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ABSTRACTS

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X-ray Peculiarities in Mental Deficiency.—The material for this paper was obtained at the Polk State School which has over 3,000 inmates, 18 per cent of whom are morons, 67 per cent imbeciles and 11 per cent idiots. About 200 are mongolians. Morons do not have a higher incidence of tuberculosis than is usual among mentally normal persons, but they exhibit a different reaction to tuberculous infection. This is also true of the high-grade imbecile. In the low-grade imbecile and idiot there is a marked difference in the lung findings. A much larger amount of perivascular infiltration is seen, which is present throughout the lungs but is most marked at the bases. Mottled areas of congestion may be seen in any portion of the lower two-thirds of either lung. Thus, in making a diagnosis, one must know the mental level of the person X-rayed. The reason for this difference is open to conjecture. One that is advanced is that the low-grade imbecile and the idiot have a low cough threshold, for they will cough only if the irritation is severe, but phlegm or mucus in the upper respiratory tract gives them no concern. Some of these patients lead very sedentary lives, their mentality being such that all they do is sleep and eat. In those more active there seems to be less perivascular infiltration and congestion. The musculature in the more apathetic is very flabby and gives an unusual X-ray appearance. Lateral portions of the chest show band-like shadows of the latissimus dorsi and pectoral muscles and the outer and upper thirds of the lung show much greater penetration than is usually the case because of the lack of muscular density. Body deformity often accompanies mental deficiency so that many cases of thoracic cage deformity are found and atelectasis, congestion and chronic infection may be seen as a result of the deformity. In spastic paralysis there is an increased amount of infiltration in the lungs roughly corresponding to the degree of paralysis in the muscles of the chest. Most of these spastics are low-grade imbeciles and idiots and consequently the amount of perivascular infiltration would be even greater. Mental defectives will also swallow huge amounts of air, which fills the stomach and bowels and results in an elevation of the diaphragms and compression of the lungs. All mental defectives have no resistance to tertiary tuberculosis. Almost all inmates show evidence of the primary complex. The amount of calcification, however, is never very great. No case of secondary tuberculosis was seen. Tertiary tuberculosis is usually seen in the early teens. It is difficult to detect without X-ray examination for the patients often are unable to speak ,or are too low in mental capacity to tell they are not feeling well. The attendant may notice that the appetite is poor and that the patient is more listless than usual. An elevation of temperature is fairly common and would not lead one to suspect tuberculosis. The first film may show no tuberculosis so that a progress film is usually made in about two weeks. This may show the beginning disease. Parenchymatous involvement is usually seen in the lower portion of the upper third of the lung. As a rule it advances very rapidly. It may be seen in both lungs on the

first examination. Fibrosis seldom occurs and is never extensive. Cavities are common. If the patient lives over three months very large cavities involving the upper portions of both lungs are often seen. Acute pneumonic consolidation is another common occurrence. While the pneumonic process is clearing the characteristic parenchymal changes become evident in other portions of both lungs. Fatal termination usually occurs at a rapid rate. A third type of disease seen, is the soft snow-flake like infiltration of both lungs from apex to base. This is rapidly fatal, the process rarely lasting longer than two months. Pulmonary hemorrhage is uncommon. A patient found to have tuberculosis usually lives only a few weeks and seldom lives more than six months. The average period of survival is around two months. The reason for the lack of resistance is not known. It is unusual to see tuberculosis associated with spastic paralysis. Mongolians have very poor resistance to tuberculosis and about 30 per cent have congenital heart disease. In a total of 185 deaths during a period of eighteen months, 57 were due to tuberculosis.—*Roentgenograms of the Chest in Mental Deficiency, J. T. Danzer, Radiology, March, 1946, 46: 244.*—(*G. F. Mitchell*)

Tuberculosis and Pregnancy.—Numerous differences of opinion as to the management of cases of pulmonary tuberculosis and pregnancy are found in the literature. The current article deals with an experience with 177 consecutive cases. Quiescent cases were encouraged to lead a life comparable to that in a sanatorium. Active cases were managed in accordance with their pulmonary disease. Artificial pneumothorax did not cause embarassment to the mother during labor. Psychological management, particularly reassurance regarding the safety of the infant, was important. Patients were divided into three groups: (*1*) arrested and recovered (no evidence of activity for over two years), (*2*) quiescent (no evidence of activity), and (*3*) progressive. Retrogression occurred in 3 out of 69 cases in group 1, 5 out of 50 in group 2 and 15 out of 58 in group 3. There was a possible tendency to premature labor in cases with active disease, but otherwise tuberculosis appeared to have little effect upon either pregnancy or labor. Follow-up studies were carried out on 120 cases for periods of six months to six years. Out of 87 quiescent, arrested or recovered cases, 2 died and 3 retrogressed. Seventeen of 58 progressive cases are known to have died. The worst cases are those which are unrecognized throughout the greater portion of pregnancy. Severe tuberculous laryngitis is considered an indication for abortion or Caesarian section at term. It is not believed that pregnancy causes sufficient change in the position of the diaphragm to exert either a beneficial effect upon the tuberculosis before labor or a harmful effect after delivery. Hence induction of pneumoperitoneum immediately after labor is not indicated. It is concluded that the number of cases showing retrogression was not greater than what would be expected in a comparable group of nonpregnant women. While it is reasonable to advise avoidance of pregnancy for one to two years after arrest of the disease, interruption of gestation ordinarily is not indicated. Patients with quiescent disease who had been treated by collapse therapy seemed to have a better prognosis than those who had been treated by conservative measures. In advanced cases the decision as to continuation of the pregnancy must be influenced by social factors, the desire for a baby, etc.—*Pulmonary Tuberculosis and Pregnancy, R. Cohen, Brit. J. Tuberc., January, 1946, 40: 10.*—(*A. G. Cohen*)

Pathophysiology of Exudative Tuberculosis.—Disturbances in the neuro-regulation of the circulation in the lung play a decisive rôle in the formation of exudative reactions. Stimulation of the sympathetic adrenergic nerve fibers produces a constriction of the pulmonary vessels. Inhibition of these fibers produces an increased dilatation of pulmonary vessels. The parasympathetic cholinergic fibers act essentially on broncho-constriction, increase the tonus of the smooth muscles of

the lung and act on the contractility of the lung. Acetyl-cholin has a similar effect. On the whole, the sympathetic and parasympathetic innervation of the lung has a "defensive" rôle, increasing the resistance towards inflammation. Paralysis of the vagal and sympathetic innervation intensifies hyperergic inflammations. Investigations on the reactivity of the vegetative nervous system during a progressive phase of tuberculosis reveal signs of insufficiency of the sympathetic as well as the parasympathetic tonus, manifesting itself especially in the vascular reflexes. Under the conditions of congestion, infiltration and exudation blood- and lymphstasis develop due to vasodilatation and paralysis of the smooth muscles of the lung parenchyma. The treatment during an exudative phase of tuberculosis has to pursue the aim of reducing vasodilatation, of decreasing the permeability of the capillaries, and of increasing the contractility and the turgor of the lung as a whole. Pneumothorax refills are believed to act in this direction, by stimulating the parasympathetic nerve endings in the pleura and producing a pleuro-pulmonary reflex. (Liberation of acetyl-choline leads to active contraction of the lung, which produces considerable decrease of its blood and lymph depots.) In addition to cholinergic and adrenergic fibers, histaminergic fibers play a rôle in regulating the vascular system of the lung. Their stimulation produces dilatation of capillaries, increase in permeability and local exudative reactions. Histaminergic fibers are carried in the phrenic nerve. The effect of the usual interventions on the phrenic nerve is believed to be due not only to mechanical factors but also to an effect on the vascular system of the lung, by eliminating the influence of histaminergic fibers. —*Questions of Pathophysiology in the Therapy of Exudative Exacerbations in Tuberculosis, L. M. Model, Probl. tuberk., 1945, 3: 13.*—(*V. Leites*)

Ulcero-atelectatic Syndrome.—A cavitary lesion in an apex, usually on the left side, associated with atelectasis of the entire lung, represents a well defined clinical and roentgenological entity. A massive density occupying an entire lung may be due also to a pleurogenic sclerosis, to a chronic sclerotic pulmonary lesion or to caseous pneumonia. When possible, a manometric reading in a free pleura will show highly negative pressures in the presence of an atelectatic lung. The diagnosis of atelectasis can be made also retrospectively, rapid clearing of a consolidated lung occurs along with the disappearance of the signs of retraction of the hemithorax. A long standing atelectasis causes irreversible changes in the lung. On reviewing 2,000 cases (1,200 males and 800 females) 18 cases were found (0.90 per cent) where a diagnosis of ulcero-atelectatic syndrome could be made; 13 cases were observed on the left side, 5 cases on the right. The greater incidence of the atelectasis on the left side can be explained by the position of the left bronchus in respect to the left pulmonary artery. Fourteen cases were found in women and 4 in males. The incidence of this syndrome was greatest in the age group from 21 to 30. The atelectasis usually occurs without marked toxemic or functional symptoms. The cavitary component of the syndrome is not always visible on the plain X-ray film; tomographic studies or Bucky technique are sometimes necessary to reveal its existence. The prognosis is usually poor, because, in spite of the slow clinical course, there is an active process which in due time will lead to bilateralization or extensive permanent structural change in the lung which may in their turn be the cause of cardiac failure. Pneumothorax is usually contraindicated, occasionally it may be of some temporary use. Thoracoplasty is the procedure of choice, unless it be contraindicated for other reasons.—*Sindrome ulcero-atelectasico, D. Mazo, An. Fac. de cien. med. (Paraguay), June, 1945, 5: 55.*—(*L. Molnar*)

Negative Tuberculin Reaction in Active Tuberculosis.—The chest roentgenogram of a 23 year old man showed exudative lesions with cavitation in the right upper lobe with spread to the left upper lobe. The patient's general

condition was good. The sputum was positive for tubercle bacilli on direct smear and in the animal experiment. The Pirquet and Mantoux (with 5 mg. tuberculin) tests were negative. A right pneumothorax was induced and the sputum turned negative. Repeated Mantoux tests with tuberculin up to 10 mg. were negative. To a cutaneous BCG vaccination the patient reacted with accelerated focal papular lesions already two days after vaccination in a manner less violent than a tuberculin-positive individual (Koch-phenomenon), while a noninfected tuberculin-negative person reacted with focal papular lesions two weeks after the cutaneous BCG vaccination. This is considered a case of iathergic immunity, in which tuberculin hypersensitiveness is eliminated while immunity is retained.—*Concerning Negative Tuberculin Reactions in Active Pulmonary Tuberculosis: Does Immunity Persist in the Absence of Cutaneous Allergy?, J. Solem, Acta med. Scandinav., November 12, 1942, 112: 435.*—(*G. C. Leiner*)

Lower-lobe Tuberculosis.—Among 768 cases of pulmonary tuberculosis, 15 (2 per cent) showed basilar involvement. There were more cases of right sided involvement than left and more in females than in males. It is believed that the condition is caused by a rupture of a caseous node into a bronchus. This theory is based upon 3 features in the history of these cases: (*1*) acute onset following a chronic cough; (*2*) high incidence following primary pleural effusion and (*3*) history of vague ill-health associated with a dry cough. The prognosis is poor because of: (*1*) acute onset, (*2*) late diagosis and (*3*) relative ineffectiveness of artificial pneumothorax and phrenic paralysis. Pneumothorax was ineffective in the 11 patients in whom it was tried. Phrenic paralysis was ineffective in all until supplemented by pneumoperitoneum. With the latter, there was cavity closure and clearance of atelectasis in 10 cases; in 2, the cavity closed but atelectasis persisted; in the remaining case, the cavity did not close. Absorption collapse was noted in 5 cases prior to collapse therapy and in 4 after pneumothorax. Five of these also showed enlarging cavitation. Following phrenic paralysis and pneumoperitoneum, there was reaëration in 7. In the other 2, the collapse persisted and endobronchial lesions were found.—*Basal Pulmonary Tuberculosis with Special Reference to Aetiology and Treatment, F. S. Hawkins & G. O. Thomas, Tubercle, July, 1946, 27: 82.*—(*A. G. Cohen*)

Lower-lobe Tuberculosis.—The author reviewed 2,200 cases of pulmonary tuberculosis treated in a sanatorium in a nine-year period, abstracting those in which the disease was solely or predominantly affecting the lower lobe on one side. Only 81 such cases (3.68 per cent) were found. Cases of bronchogenic spread from the upper lobes were excluded. The incidence on the two sides did not show any significant difference (48, right; 33, left). In 34(42 per cent) the apex of the lower lobe was affected; and 32 of these had progressed to cavitation. Three groups were differentiated radiologically: (*1*) 21 cases—those showing tuberculous infiltration, including diseases of exudative type, with no demonstrable cavity formation. Sixteen of these were treated by an initial period of bed-rest, which secured quiescence in 11; pneumothorax was induced in 4 of the resistant cases with ultimate quiescence; of the remaining cases 3 had a successful pneumothorax, one responded well to a phrenic avulsion and the other to intravenous gold. (*2*) 28 cases, those showing cavity formation, but excluding those in which the cavity occurred at the apex of the lobe; 4 were treated by bed-rest, 2 responding well and one of the remaining 2 successfully treated with pneumothorax subsequently; 13 cases were treated initially with pneumothorax, 10 succeeding and 2 were abandoned due to spread; phrenic paralysis alone succeeded in 7 of the 10 cases, the 3 failures subsequently becoming quiescent after pneumothorax, (*3*) 32 cases, those in which a cavity had formed at the apex of the lower lobe; 10 of these cases, in which the apical cavity was small, were treated by bed-rest alone, 8 successfully; of 16 cases treated

by pneumothorax complete quiescence was secured in 12, one had to be reinforced by a phrenic paralysis and 3 failed entirely; 5 cases were treated by early phrenic paralysis, 3 succeeded and 2 failed. The results were good in the first two groups, but where the cavity was at the apex of the lower lobe only 25 cases became quiescent out of 32. The probable explanation of this is that when the lung is collapsed the apex of the lower lobe moves into the paravertebral gutter and escapes compression. Among the conclusions gathered from these studies were: (*1*) the low incidence of lower-lobe tuberculosis; (*2*) the distinct tendency to early cavity formation; (*3*) the immediate prognosis with adequate treatment is better than has usually been thought; (*4*) if cavity is already present, bed-rest should not be prolonged before other treatment is started; (*5*) for non-apical cavities phrenic crush with pneumoperitoneum should be tried; and (*6*) where the cavity is at the apex of the lower lobe an initial pneumothorax seems to be the best treatment.—*Tuberculosis of the Lower Lobe, R. C. Cohen, Brit. M. J., May 12, 1945, 1: 662.*—(*D. H. Cohen*)

Lower-lobe Tuberculosis.—During a period of eighteen months, there were 4 cases of purely basal tuberculosis in approximately 90 admissions. The criterion for selection was limitation of the lesion to the lower half of one or both lungs. Twenty-five cases were seen during twenty-three years. Limited diaphragmatic excursion is offered as a partial explanation for localization in the lower lobes; evidence for this belief is furnished by the greater incidence of basal lesions in females and in the right lung. Prior to the widespread use of X-ray examinations, basal pulmonary lesions were presumed to be non-tuberculous unless tubercle bacilli were found in the sputum. Therefore statistical reports based on physical examination alone are not accurate. However, a summary of over 25,000 published cases indicates an incidence of 1.5 per cent. It is believed that the prognosis is poor. Generally, cavitation and bronchogenic spread occur, particularly in untreated cases or those treated by bed-rest alone. Where thorough collapse measures are employed, the results are more satisfactory. Pneumothorax treatment is often effective. However, fluid formation is more likely to nullify the results than in cases with upper lobe lesions. Where uncuttable adhesions to the diaphragm are present, combined pneumothorax and phrenic paralysis are often effective. Phrenic paralysis as an initial procedure is beneficial in relatively few cases. However, when supplemented by pneumoperitoneum, the results are much more striking. Relatively few cases have been treated by thoracoplasty but the results have been good. The chief objection is the necessity of sacrificing so much healthy lung tissue. For physiological reasons, thoracic surgeons do not consider lower thoracoplasty to be a good operation.—*Basal Tuberculosis, P. Steen, Brit. J. Tuberc., January, 1945, 39: 3.*—(*A. G. Cohen*)

Blood Prothrombin in Tuberculosis.—The prothrombin content in the blood of 101 patients with pulmonary tuberculosis was found to be within the normal range when compared with 50 healthy persons. The tests were made by means of Plum and Larsen's modification of Quick's method on venous blood. The prothrombin content in the blood of 17 patients with hemoptysis was found to be normal. The administration of large doses of synthetic vitamin K to 4 normal persons and 10 patients with pulmonary tuberculosis produced a slight, probably unimportant increase in the prothrombin content in the blood. It is believed that there is no indication for the use of vitamin K in cases of hemoptysis.—*Prothrombin Content of the Blood in Pulmonary Tuberculosis, P. Plum & J. E. Poulsen, Acta med. Scandinav., November 12, 1942, 112: 426.*—(*G. C. Leiner*)

Tuberculous Bronchitis.—This term is often applied to all cases showing clinical or bronchoscopic evidence of bronchitis without a clear definition of the pathological anatomy. Four

different forms of bronchitis can be distinguished in the course of turbeculosis. True tuberculous bronchitis or tracheobronchitis is due to involvement of the major airways by tuberculous disease. The result is a very characteristic clinical picture which consists of fairly constant physical signs, a bacilliferous sputum, even in the absence of major parenchymal changes, and often associated with partial or total collapse of a lung or portions thereof. The prognosis of this condition is very guarded and collapse therapy in cases with concomitant parenchymal disease is beset with dangers. Nonspecific bronchitis often accompanies active pulmonary tuberculosis. This condition is subject to frequent exacerbations and regressions. The periods of activity are characterized by increase in cough and expectoration, increase in the physical signs in the chest, and a slightly elevated temperature. The condition is due to irritation of the bronchial mucosa by infectious pulmonary secretions. Symptomatic and climatic therapy can ameliorate the condition. True allergic bronchitis is not uncommonly seen in connection with tuberculosis. The sputum is tenaceous and contains eosinophils. It is treated like bronchial asthma. Finally, bronchitis is a frequent occurrence in failure of the lesser circulation. Pulmonary fibrosis and pulmonary hypertension cause symptoms of bronchitis such as are commonly seen in congestive heart failure of marked degree. The treatment is that of heart failure, and administration of digitalis and bed-rest are the foremost therapeutic procedures.—*Die "tuberkulöse" Bronchitis, H. Alexander, Schweiz. med. Wchnschr., January 19, 1946, 76: 47.*—(*H. Marcus*)

Draining Bronchi.—The roentgen appearance of the lung between a present or former tuberculous cavity and the hilum is of importance because of the intervening structures, especially the lymph channels and bronchi draining this area. The draining bronchi are frequently involved and it is believed that the X-ray appearance, as well as bronchoscopic findings and circumstantial evidence, may be sufficiently characteristic to permit an opinion as to their status. Reports of roentgenographic studies previously made are so accurate and in agreement with every day practice of roentgenography in a tuberculosis hospital that the X-ray appearance of these draining bronchi should be more generally known. Ameuille and Févesque describe diseased bronchi as being visible between the cavity and hilum as two, usually parallel lines of opacity. Wolf confirmed these findings and published excellent roentgenograms to demonstrate them. Recently there has been increased clinical interest in such bronchi, as it is recognized that the course of the cavity is inextricably bound to the condition of the draining bronchus. Coryllos emphasized the importance of such bronchi and described the so-called stem cavities. The mode of involvement of the bronchi is not exactly known, but the simplest explanation is that they are involved by direct extension from the cavities they drain and by direct implantation from the infected material draining through them. The roentgen appearance will vary with the severity and duration of the underlying disease and may persist after the active parenchymal disease has subsided. Early, there may simply be increased visibility of the bronchial shadow and rapid clearing may occur leaving no detectable roentgen shadow. The clearing of such a shadow suggests either a nonspecific process or minimal tuberculosis. Later, when there is an associated submucous extension and infiltration, the visibility of the bronchial shadows is further increased and can often be noted even when disease in contiguous areas tends to obscure the process. At this stage it appears as two closely parallel lines separated by a central shadow. It is the opinion of the majority of pathologists that the dependent portion of the trachea over which most of the infected material passes is the site of greatest disease and tomography of draining bronchi with thickened dependent walls suggests that the same is true for bronchi. When infection extends through the mucosa producing ulceration and

irregular granulomatous lesions with continued extension along the bronchial wall, the bronchial shadow will be denser, more irregular and wider in diameter, while the lumen will be narrower and irregular. Peribronchial reaction in the adjacent tissue may occasionally be seen as a soft "exudative" shadow lying between the cavity and hilum. Though the bronchial shadows are not identifiable, the shadow between the cavity and hilum must be attributed to the regional bronchial and peribronchial disease. Such a bronchus, visualized only at one end by the bronchoscopist, may be demonstrated in its entirety by the roentgenologist. If the ulcerogranuloma completely fills the bronchus, peripheral atelectasis may occur. At this stage, when caseous endobronchitis occurs, the bronchial and peribronchial shadows will be even more pronounced. In some cases several bronchi may drain a larger area of involvement. Resolution of tuberculous bronchitis is usually associated with some fibrous change. Roentgenographically there is diminished visibility of the bronchial shadow but, if the disease has been extensive, fibrotic residua are seen as well demarcated linear fibrotic strands extending from the hilum out into the lung fields. If the pulmonary disease becomes worse, it will be reflected by the advance of the chronic changes in the bronchial walls characterized by rigidity, straightening and shortening. This is associated with varying degrees of stenosis which may contribute to bronchiectatic changes in the peripheral arborization. The presence of linear bronchial markings which extend into the lung field from the hilum should lead to the suspicion that a hidden cavity is being drained and careful search should be made. In the complicated cases with extensive parenchymal disease, diseased bronchi may be picked out. Tomographic studies are of great value. When these are not available, Bucky studies are very informative.—*Roentgenology of the Draining Bronchi from Tuberculous Cavities, M. R. Camiel, Radiology, January, 1946, 46: 24.*—(*G. F. Mitchell*)

X-ray Appearance of Draining Bronchi.—Among 3,000 X-ray films of pulmonary tuberculosis 30 cases with rontgenologically demonstrable draining bronchus (1 per cent) were found. This image was always situated in the upper lobes. In most cases the outline of the bronchus was irregular, sinuous, with thickened borders. It originated from the lower pole or the lateral wall of the cavity. Bronchoscopy performed in these cases confirmed the presence of endobronchial disease. The observation was made that pneumothorax in patients presenting the image of a draining bronchus was more frequently followed by complications than in patients without this X-ray finding. Among the 30 cases pneumothorax was attempted in 25. The attempt was unsuccessful in 68 per cent (no free pleural space or contraselective pneumothorax). Ballooning of cavities and perforations occurred in 28 per cent of cases.—*L'image radiologique des bronches de drainage et son intérèt pour le pronostic de la collapsothérapie, M. Bariéty & J. Paillas, Rev. de la tuberc., 1944-45, No. 10, 9: 216.*—(*V. Leites*)

Hemoptysis.—An analysis was made of 416 cases in which hemoptysis occurred. There were 161 cases of tuberculosis (39 per cent), of which 133 were active. Conversely, 15 per cent of all tuberculosis patients had hemoptysis. Of these, 27 per cent had small, 48 per cent intermediary and 25 per cent extensive lesions, indicating that the presence of hemoptysis is no indication of severity. Moreover, there is no correlation between the amount of bleeding and the extent of the lesions. The next most common causes, in order of frequency were chronic bronchitis, bronchiectasis and inactive tuberculosis. In the latter condition, associated bronchiectasis is the most likely cause of the bleeding. The list of causes included about 20 other conditions. There were 66 cases (16 per cent) in which the cause of the hemoptysis could not be ascertained.—*The Significance of Hemoptysis, R. J. Heller, Tubercle, May—June, 1946, 26: 70.*—(*A. G. Cohen*)

Atelectasis after Hemoptysis.—A case of transient atelectasis after hemoptysis is described. A young man suffered an abundant hemoptysis. A dense homogeneous shadow was found in the extreme lower right portion of the lung with retraction of the hemithorax and some mediastinal displacement. The next day this picture had completely disappeared. At all times his sputum was negative for acid-fast bacilli. Subsequent X-ray films did not show any trace of the previously observed lesion. Most cases found in the literature describe a posthemorrhagic bronchial obstruction with atelectasis of an entire lung or of one lobe. The peculiarity of this case is that only a portion of the right inferior lobe was affected. This also explains why there were no functional symptoms, such as sudden dypsnea, thoracic pain, etc. It was just by accident that this transient atelectasis was discovered. There may be many cases which are never found unless fluoroscopy and radiography are daily routine. —*Atelectasia y hemoptisis, R. Mosera & J. Norman, Rev. de tuberc. d. Uruguay, June, 1945, 13: 299.*—(*W. Swienty*)

Insufflated Hydatid Cyst.—The case of a young man who suddenly experienced severe dyspnea, cough and chills is described. The patient did not recall having had any vomitus or to have coughed up fragments of membrane. A hydro-aërated cavity was found occupying the entire lower third of the right chest. When the cavity was entered a positive pressure of 14 cm. of water was encountered. When the patient coughed this pressure rose to 140 cm. A diagnosis of hydatid cyst was made. The cavity was evacuated and the membranes removed. The patient made an uneventful recovery. This is another example of insufflation of a hydatid cyst. If an opening in the membrane occurs and the liquid is partly or completely evacuated, the membrane may cleave to the bronchus. A ball-valve mechanism is so established. Emptying of the cavity by bronchoscopy is impossible as the hydatid cyst generally occupies the peripheral zones of the lung inaccessible to endoscopy. The method of choice is surgery with external drainage.—*Neumoquiste hidatico insuflado, R. A. Piaggio Blanco & E. J. Canabal, Rev. de tuberc. d. Uruguay, June, 1945, 13: 303.*—(*W. Swienty*)

Hepatitis and Tuberculosis.—Thirty-one cases of epidemic hepatitis were observed in a Tuberculosis Sanatorium situated on one of the Canary Islands between 1943 and 1945. During this period about 400 patients were hospitalized. The incidence of morbidity was 7.5 per cent. There occurred only one case of epidemic hepatitis among the 80 persons constituting the personnel of the Sanatorium during the same period. The spread of the infection was sporadic and disclosed nothing about the propagation of the infection. The morbidity was markedly increased during the winter. In 12 cases the patients recovered in less than two weeks; in 9 cases the duration of the disease was less than one month, in 8 cases it lasted more than one month and less than one and a half months. The clinical course was favorable in all cases. The frequent symptoms were as follows: gastrointestinal complaints, anorexia, fever, hepatomegaly. The incidence of hemoptysis was low during the course of the disease, and even afterwards less cases of hemoptysis were noted in this group of patients than in the period preceding it. Vitamin K and C were given to every patient in this group and this precaution may account for the reduction in the incidence of hemoptysis during a complication which would be expected to increase the tendency to bleeding. The sedimentation rate was very little modified by the epidemic hepatitis. The inhibitory action of the high blood level in biliary acids on the sedimentation rate may explain this phenomenon. The pulmonary disease has shown some modification under the impact of this intercurrent infection only in 7 cases (22 per cent). In 5 cases the effect was unfavorable, while in 2 cases it appeared to be favorable. It was evident that lesions of an unstable character have shown more unfavorable changes than those of a more stable type. In 2 cases pleural

effusion developed. The intensity of the icterus and of the general symptoms has had no demonstrable influence on the tuberculous process. Due to lack of laboratory facilities no data are available about the functional status of the liver during the disease and following it.—*Hepatitis epidemica and tuberculosis, T. Cervia & V. Gutierez, Rev. españ. de tuberc., December, 1945, 14: 891.—(L. Molnar)*

Avian Tuberculosis in Man.—Human tuberculosis due to avian bacilli is rare. Only 14 to 20 authentic cases have been reported, and of these only 3 had pulmonary tuberculosis. The present case report concerns a 59-year old male patient who was observed from 1942 to 1945. The clinical and roentgenological features of the disease were identical with the usual human infection, and the true nature of the bacillus was only discovered because of routine typing of all specimens received in the author's laboratory. Animal experimentation in different laboratories abundantly confirmed the fact that the organism was of the avian variety. The patient declined treatment when first observed, and when he was last seen he had far advanced cavitary tuberculosis. The patient was negative to doses of Old Tuberculin up to 1 in 1,000, but he was positive to a very dilute solution of avian tuberculin. The patient's occupational history did not seem to bring him in contact with avian tuberculosis, but inquiry into his habits revealed that he had eaten a raw egg, beaten up with milk, daily for the past thirty years. Raw eggs have been shown to contain living avian tubercle bacilli, and the author finds it reasonable to assume that his patient became infected in this way.—*Human Pulmonary Tuberculosis Due to Avian Tubercle Bacilli, F. C. S. Bradbury, Lancet, January 19, 1946, 250: 89.—(H. Marcus)*

Ventricular Deflections in Tuberculosis.—Twelve cases out of 18,500 admissions in the last ten years at the Sea View Hospital showed concordant downward initial ventricular deflections in the four standard leads of routine electrocardiograms. These 12 histories are presented. In 10 cases, downward QRS deflections were represented by S waves; the 2 cases where Q waves caused the abnormal QRS complex were both cases of acute coronary thrombosis. Of the 4 deaths in the group of 12 patients showing this electrocardiographic peculiarity, 2 were due to coronary thrombosis (mentioned above) and 2 were from patients with advanced pulmonary tuberculosis. An EKG showing concordant downward QRS complexes due to S waves is certainly not indicative of heart disease, nor does it carry a grave prognosis, as formerly thought. The phenomenon is apparently a function of heart position, as it can be influenced by varying the patient's position, by mediastinal shift, pneumothorax, mediastinal adhesions or pleuritis. Where the abnormality is due to Q waves, however, the causal coronary thrombosis conditions the prognosis. —*The Significance of Concordant Inverted Initial Ventricular Deflections in the Electrocardiogram of Patients with Pulmonary Tuberculosis, T. T. Fox, D. D. Sokol & I. J. Bernstein, Quart. Bull. Sea View Hosp., April, 1946, 8: 95.—(P. Q. Edwards)*

Bed-rest.—A group of patients with pulmonary tuberculosis, too far advanced for collapse-therapy, was observed on strict bed-rest. Since most of them chose the supine position, cavities which are most frequently in the posterior portion of the lungs, were poorly drained, cough increased, intrabronchial dissemination was freqeuent and toxemia became worse. Thereafter, patients were instructed to change from supine to prone to lateral position at frequent intervals, with emphasis on the most comfortable position and that assuring best drainage. Clinical evidence of bronchospasm was treated by bronchodilator drugs, and patients with viscous sputum were given steam-inhalation. Muscular relaxation was taught so that "an amazing degree of relaxation usually could be mastered." "Breathing decreased somewhat in rate and became perceptibly more shallow." ". . . . and rest in bed actually became

pleasurable." Attention was paid to the usual emotional problems and maladjustment in the form of humane interest and encouragement, but no mention is made of specific psychotherapeusis. "In this way, a concept of bed-rest was evolved which was based on three fundamental modalities: adequate drainage, muscular relaxation and mental repose." So far, 69 patients were treated by this regimen, frequently complemented by special diets and parenteral administration of protein hydrolysates, when indicated. Cavity closure with sputum conversion was observed in 28 per cent; in 14 per cent thoracoplasty became possible; 15 per cent have died. "Altogether, 42 or 48 per cent, have either successfully controlled their disease or have healed it to the point where thoracoplasty could be undertaken." Five representative case reports with roentgenograms are appended.—*The Modalities of Bed Rest, W. M. Peck, Pub. Health Rep., May 3, 1946, 61: 626.*—(*M. Pinner*)

Rehabilitation of Tuberculosis Patients.—It is pointed out that the volume of rehabilitation work is entirely inadequate and that this is, presumably, an important reason for reactivations. Six different types of rehabilitation schemes, which are in existence in America and abroad, are briefly discussed. The legal machinery available for rehabilitation work is described and the full utilization of state projects is recommended. "The success of each of the four objectives of the Tuberculosis Control Division of the United States Public Health Service—case finding, treatment and isolation, after-care and rehabilitation, and protection against economic distress—is dependent on the success of each of the others."—*Rehabilitation and After-care in Tuberculosis, H. E. Hilleboe & N. C. Kiefer, Pub. Health Rep., March 1, 1946, 61: 285.*—(*M. Pinner*)

Treatment of Hemoptysis.—Hemoptysis in tuberculosis was treated by the induction of artificial pneumomediastinum. The suprasternal notch was anesthetized. An ordinary refill needle was bent 4 cm. from the point, forming an obtuse angle. The needle was introduced downwards along the posterior surface of the sternum for a distance of about 4 cm. The stilette was then removed. The needle was connected to a pneumothorax apparatus. The initial pressure was plus 14, plus 16. After 200 cc. of air were introduced, the pressure was lower. Bleeding stopped after 500 cc. had been given. The only complications were slight fever and subcutaneous emphysema in the neck.—*Artificial Anterior Pneumomediastinum in the Treatment of Haemoptysis, J. M. Velasco, Tubercle, July, 1946, 27: 95.*—(*A. G. Cohen*)

Phrenic Nerve Paralysis.—The view is expressed that phrenic nerve paralysis is effective only in lesions located within lung areas subjected to mechanical tension during diaphragmatic motion. The mechanical influence of diaphragmatic excurisons is essentially limited to the lower lobes, but is transmitted to the upper lobes in case of interlobar adhesions. A diagnostic aid is proposed in order to facilitate the indications of phrenic nerve paralysis. The "synergistic indicator" consists in determining the displacement of lesions on fluoroscopy during exclusively diaphragmatic respration (with voluntary elimination of costal respiration). The sign is considered positive if the displacement of the lesions follows the direction of the diaphragmatic movements. These cases are considered good canidates for phrenic nerve paralysis in contradistinction to those in whom this sign is absent. Thus, the "synergistic indicator" would make it possible to detect the presence or absence of a mechanical connection between the involved lung area and diaphragmatic excursions and to recognize lesions as belonging to the lower lobes in spite of their projection into the upper lung-fields on the posterior-anterior film. (No mention is made in this context of the use of lateral views as a means of localization.) Patients operated upon according to the indications of the synergistic phenomenon are said to have had good results in the great

majority of cases (closure of cavities, clearing of infiltrations, conversion of sputum). However, the definition of a "good" result is explicitly limited to a favorable effect only on the area influenced by diaphragmatic motions. Spreads and progressions of disease in other areas of both lungs occurring at a later date are deliberately excluded from the discussion with the argument that they do not disprove a success of the intervention as a procedure aiming at a local effect only.—*The Synergistic Indicator in Phrenic Nerve Paralysis, V. A. Rabich-Shchebro & N. N. Ignatowskaja, Probl. tuberk., 1945, 4: 33.*—(*V. Leites*)

Phrenic Nerve Paralysis.—In the twenty-year period from 1926 to 1945, 122 cases of pulmonary tuberculosis were treated by phrenicoexeresis; 67.2 per cent of the patients died during the period of observation, 15.5 per cent were lost out of sight during the first three years after the intervention and 17.2 per cent showed improvement or were "cured" after three years from the operation. Phrenicoexeresis was the sole collapsotherapeutic procedure in 75 cases; only 2 of these cases were considered apparently cured at the end of the three year period. In 47 cases phrenicoexeresis was associated with pneumothorax, thoracoplasty or pneumoperitoneum. The late results of these combined procedures were also poor. It is significant that, while the number of phrenicoexeresis has constantly decreased during these twenty years, the cases of thoracoplasty have shown a considerable and constant increase during the same period. The age of the patients has had no visible influence on the outcome of the operation. The results were not significantly better in the cases performed during the latter part of the period in question, thus proving that the experience accumulated during the first years failed to provide a safe basis for correct indications. The same can be said of the degree of elevation of the diaphragm, of the topography and the nature of the lesions. In view of the poor results and of the uncertainty of the criteria in the indication and in the prognosis, phrenicoexeresis has a limited place in the treatment of pulmonary tuberculosis.—*Veinte anos de experiencia en el tratamiento de la tuberculosis pulmonar por la frenicoparalisis, F. D. Gomez, J. C. Negro & R. Burgos, Hoja tisiol., March, 1946, 6: 36.*—(*L. Molnar*)

Artificial Pneumothorax.—An important rôle is attributed to active contractility of the lung, dependent on the action of its smooth muscle fibers. This mechanism is believed to explain the frequent observation that on the day after induction of pneumothorax a greater degree of collapse is present than would correspond to the amount of injected air. The current explanation of this phenomenon as due to puncture of the lung is considered improbable by the authors. In 112 cases of initial pneumothorax 49 showed a disproportionately large pneumothorax space. In all cases the injected air was passed through a filter saturated with peppermint. Only 5 out of the 49 cases perceived the odor of peppermint after the refill, and judging according to other signs they presented a genuine traumatic pneumothorax. The other 44 patients did not perceive any odor and it is concluded that the additional collapse had another cause than puncture of the lung. The assumption is made that the mechanical irritation of the lung during the initial refill produces a spasm of the smooth muscles of the lung with relaxation of the bronchial muscles, followed by considerable fall in the partial pressure of gases in the intrapleural space and with corresponding diffusion of gases from the blood vessels into the pleural space. In contradistinction to patients with traumatic pneumothorax, these patients showed that rapidly after the refill the carbon dioxide concentration in the pleural space corresponded to the concentration in the venous blood. In 52 cases the volume of the pneumothorax space was determined by the method of injecting pure carbon dioxide and analyzing its dilution. If measured twenty-four hours after the refill only 3 cases revealed the pleural space to contain

approximately the same quantity of gas as has been injected. In all remaining cases the pleural space contained about the double amount. The state of the smooth muscles of the lung is considered to be at the basis of another phenomenon in artificial pneumothorax. It is believed that cavities remaining open under pneumothorax fail to close because of "atony" of the pericavitary lung tissue. Contraction of a certain number of such cavities after intrapleural injection of different substances (oil, saline) is taken as evidence for the appearance of a reflex spasm of the smooth muscles after pleural irritation. —*Investigations in the Field of Artificial Pneumothorax, F. A. Michailow, Probl. tuberk., 1945, 2: 19.*—(*V. Leites*)

Artificial Pneumothorax.—During a three year period, pneumothorax induction was attempted in 781 cases, 409 of which received pneumothorax for three months or more. Of these, 19 had disease classified as caseo-pneumonic, 244 predominantly exudative, 109 mixed and 37 predominantly fibrotic. All classifications were made on the basis of X-ray films. Results were best in the last group (75.7 per cent sputum conversion), while in the first three groups there was no significant difference. The extent of the disease naturally influenced the response, but it was noted that the results were about the same with involvement of one zone or two zones (recorded according to the standards of the Tuberculosis Association of India, which divides the lungs into three zones). The presence of cavities, partial or contraselective collapse, disease in the contralateral lung, diabetes, affected the prognosis unfavorably. Displacement of the mediastinum, and effusion apparently did not influence the results, while the presence of intestinal tuberculosis and the occurrence of spontaneous pneumothorax exerted an unfavorable effect.—*A Study of Certain Factors Influencing Results of Artificial Pneumothorax Treatment, P. V. Benjamin, K. T. Jesudian & R. Subramaniam, Indian M. Gaz., January, 1945, 80: 1.*—(*P. Lowy*)

Bronchoscopic Aspiration of Tuberculous Cavities.—A report is given of 6 cases with tension cavities under pneumothorax, treated with bronchoscopic aspirations. In all cases the ballooning of the cavity had occurred following pneumonolysis. Each patient received from 2 to 6 bronchoscopic aspirations separated by a time interval of two to three weeks on the average. Five out of the 6 cases showed rapid disappearance of the cavity and of the positive sputum. No relapse is said to have occurred within the next two years. The sixth case was a failure. Perforation of the tension cavity developed after the second aspiration. In 2 cases bronchoscopic aspiration seemed to have provoked a pleural effusion. The aspirations were followed by increased expectoration and rapid improvement of the general condition (fall in temperature, gain in weight). In order to be effective the bronchoscope has to be approached as closely as possible to the draining bronchus of the cavity. Endobronchial applications of adrenalin are considered to have an auxiliary effect in diminishing mucosal swelling and further improving cavitary drainage.—*La broncho-aspiration des cavernes pulmonaires tuberculeuses ballonées, J. M. Lemoine, A. Diacoumopoulos & J. Paillas, Rev. de la tuberc., 1944–45, No. 10, 9: 205.*—(*V. Leites*)

Thoracoscopy.—In a period of one year, 455 thoracoscopic examinations were made. The author believes that the preoperative roentgenogram is of no help in determining whether or not the adhesions can be divided. It is his policy to perform thoracoscopy in all pneumothorax cases where the procedure is not abandoned after two or three refills. He was unable to introduce the instrument in only one case. Even in those cases where the roentgenogram indicated very extensive adhesions, a fair proportion were helped. A total of 325 pneumothoraces were thus examined. Adhesions were completely freed in 170 (52 per cent). Satisfactory pneumothoraces were obtained in 64 (20 per cent); in these cases adhesions to the mediastinum

not higher than the sterno-clavicular joint remained uncut. Partial pneumothoraces, in which the lung remained suspended, but in which there was some degree of improvement were obtained in 11 (3 per cent). Pneumothorax was abandoned in 50 (15 per cent); no adhesions were found in 12; there were 18 cases awaiting further section. Many cases required two, three or four sessions. The author uses a single puncture direct vision thoracoscope. The instrument is introduced in the anterior axilla. He has the patient sit up after the apical and lateral adhesions have been cut. Of 18 cases where no adhesions were seen in the roentgenogram, thoracoscopy revealed their presence in 6. The following complications were noted within a three-month period after each section: pleural effusion, 15 (4.5 per cent), tuberculous empyema, 12 (3.7 per cent), hemothorax, one case.—*Comments on Total Thoracoscopy, R. Laird, Tubercle, September -October, 1945, 26: 149.*—(*A. G. Cohen*)

Pneumonolysis in Bilateral Pneumothorax.—A closed pneumonolysis done at the right moment, can improve the results of bilateral pneumothorax tremendously. The authors have done 52 Jacobaeus operations in 30 patients with bilateral pneumothorax. Of those patients, 5 had simultaneous initial bilateral pneumothorax. The results in this group were favorable in 25 and unfavorable in 5. Amongst the 5 patients with bilateral simultaneous initial pneumothorax, 4 improved considerably after pneumonolysis. Eleven patients were under 20 years of age, 10 of which improved. Nineteen patients were over 20 years, of which 12 improved. Twenty-one were women and 9 were men. Eleven cases had bilateral lesions from the beginning; 12 had contralateral involvement after pneumothorax had been induced on one side. Of the 30 cases, 23 had a complete severance of adhesions; 18 had favorable results. Of the 7, in whom not all adhesions could be cut, only 4 had good results; 14 patients had a pneumonolysis on both sides with good result in 10; 16 patients were operated on one side only with good results in 12. Of the complications observed, one patient had intense dyspnea and cyanosis; 13 had a slight polypnea; 15 had some emphysema; 10 had a slight pleural effusion. One had bilateral pleural fluid and a bronchopleural fistula on the contralateral side and one had a complete atelectasis of the operated lung. In the opinion of the authors, pleural ahesions, which are the most frequent reason for inefficiency of bilateral pneumothorax, should be operated early by closed pneumonolysis. This operation is without special risks. It is very important to evaluate the vital capacity correctly. The outcome of the operation depends upon the vital capacity, the fixation of the mediastinum, the intrapleural pressure which should always be subatmospheric and the condition of heart and circulation. After the operation it is important to suppress cough and sometimes it may be necessary to aspirate some air from the pleural cavity. If, during the treatment with artificial pneumothorax, it is necessary to start a pneumothorax on the contralateral side, it is better to do the pneumonolysis before instituting the contralateral pneumothorax.—*Resultados de la operacion de Jacobaeus en el neumotorax bilateral, F. A. Medici & R. Sampietro, Rev. méd. peruana, July, 1945, 18: 231.*—(*W. Swienty*)

Intrapleural and Extrapleural Pneumothorax.—In a large number of cases of pneumothorax, the presence of inseverable adhesions necessitates abandonment of the procedure. In such cases, thoracoplasty generally is the next step. However, when there is rather widespread disease in the affected lung, or involvement of the other lung, thoracoplasty is not the ideal procedure. As an alternative, combined intra- and extrapleural pneumothorax has been proposed. Without abandonment of the intrapleural pneumothorax, an extrapleural space is created over the adherent portion of the lung. This is done under local anesthesia. The wall between the intra- and extrapleural cavities is cut through, thus creating a single

cavity. Refills are then given, as in intrapleural pneumothorax. In the 5 cases so treated, an excellent collapse was obtained in every case. The most troublesome complication was the formation of exudate, which, in some cases, became purulent and resulted in one fatality.—*Combined Intra- and Extrapleural Pneumothorax, "Pneumothorax Mixte," S. Berg, Acta med. Scandinav., 1946, Supp. 170: 408.*—(*A. G. Cohen*)

Postpneumothorax Bronchospirometry.—Since pneumothorax treatment is now being used quite extensively (in Scandinavia) for minimal parenchymal involvement and even for exudative pleuritis, the question of postpneumothorax function of the healthy lung tissue on the treated side becomes one of considerable significance. Bronchospirometric studies intended to test function of the lung in discontinued pneumothoraces in comparison with the normal contralateral lung showed a great variation in results. Impaired function of the treated lung may be due to changes incident to healing of the tuberculous foci and/or conditions directly connected with the pneumothorax; *e.g.*, exudative pleuritis during the course of treatment may be ascribed to one or both causes. It is therefore not always possible to decide the causal relationship of impaired function. Uncomplicated pneumothoraces of average duration do not produce any appreciable diminution of function. Patients who have had pleural exudate during treatment invariably have poor results: there is a close corellation between the reduction of function and the degree of pleural exudation and immobilization of the diaphragm. Oxygen consumption of the treated lung is more severely affected than the carbon-dioxide output and minute ventilation. Because of the possibility of reduced lung function, pneumothorax must not be considered a reversible collapse measure. Careful judgment must be used in evaluating the amount of tuberculosis which has to be healed against the potential reduction in function of that lung to almost nil in the event that complications arise during treatment.—*A Bronchospirometric Study of the Lung Function after Concluded Pneumothorax, T. Bruce, Acta tuberc. Scandinav., 1946, 20: 68.*—(*P. Q. Edwards*)

Pneumoperitoneum.—The history and technique of pneumoperitoneum are briefly reviewed. Oxygen, air or nitrogen are used; the frequency of refills needed decreases in the above order, owing to differences in the speed of absorption of the 3 gases. Pneumoperitoneum may be used either independently or in conjunction with, or preparatory to, other therapeutic measures. As an independent treatment, pneumoperitoneum is indicated where other types of collapse therapy are not feasible (extensive bilateral pulmonary tuberculosis, pleural adhesions, severe hemorrhage, basal bronchiectasis or emphysema, pulmonary tuberculosis complicated by intestinal or peritoneal tuberculosis, etc.). As an auxiliary measure, pneumoperitoneum is employed to supplement pneumothorax, phrenic nerve block or thoracoplasty. These latter are the cases in which pneumoperitoneum achieves its best results. Roentgenologically, the changes brought about about by pneumoperitoneum are elevation and limited motion of the diaphragms, compression of the lungs, separation of the subphrenic viscera from the diaphragms and disappearance of intraabdominal adhesions. Complications include ascites, peritoneal inflammation, air embolism, atelectasis, mediastinal emphysema, etc. Sixty-one patients treated with pneumoperitoneum were observed; in most of them other forms of collapse therapy were concomitantly used. Five illustrative cases are described.—*Roentgenological Aspects of Therapeutic Pneumoperitoneum in Pulmonary Tuberculosis, E. A. Schmidt, Am. J. Roentgenol., October, 1945, 54: 375.*—(*P. Lowy*)

Pneumoperitoneum.—The most serious complications of pneumoperitoneum are air embolism and mediastinal emphysema. These occurred 9 times in 450 cases who received 12,500 treatments. Only one of the 9 cases was fatal. The relative frequency

of air embolism in pneumoperitoneum calls for a review of the mechanisms of this complication. When it occurs in pneumothorax therapy, it is generally attributed to the entrance of air into a pulmonary vein. This obviously cannot be the case in abdominal punctures. One must postulate one of three possibilities, namely entrance of air into a systemic vein and a patent foramen ovale, or passage of air from the azygos system of veins in a retrograde fashion into the superior vena cava, the jugular vein, and the cerebral sinuses, and lastly there is the strong possibility that air may enter from abdominal or thoracic segmental veins into the vertebral plexus of veins and again into the cerebral sinuses. There were several cases that showed evidence of both pulmonary and cerebral embolism where one of the latter two possibilities may have been operative. Mediastinal emphysema was never seen to alarming degrees although this possibility exists. Air from the peritoneal cavity passes through the hiatus of the diaphram into the mediastinum, and, passing along the lung roots, may even cause interstitial pulmonary emphysema. The authors do not feel that the incidence of complications of pneumoperitoneum treatment is higher than of pneumothorax treatment, and that one should not feel deterred from administering this treatment because of fear of serious complications.—*Air Embolism and Pneumomediastinum in Artificial Pneumoperitoneum, F. A. H. Simmonds, Lancet, April 13, 1946, 250: 530.*—(*H. Marcus*)

Pneumoperitoneum.—The technique and the complications of pneumoperitoneum are briefly outlined. The complications of pneumoperitoneum are much fewer than those of pneumothorax. The diminution in vital capacity cannot properly be considered as a complication, since it is an expected and necessary therapeutic effect. Fluoroscopic control is necessary to determine the location of the insufflated air; if this is not collected under the diaphragm, but is found in the lower abdominal quadrants, the treatment is ineffectual and has to be abandoned. The results are best when previous paralysis of the diaphragm permits a selective collapse of one lung. Pneumoperitoneum may be indicated in: (*1*) highly active tuberculosis in adolescents, preliminary to successive pneumothorax; (*2*) in partially effective pneumothorax as a supportive measure; (*3*) in cases where pneumothorax in impossible, pneumoperitoneum following phrenic nerve paralysis may represent an independent form of treatment, especially if the right middle lobe or left lower lobe is involved; (*4*) finally, in certain upper lobe lesions where a cavity remains open in spite of pneumothorax, a pneumoperitoneum may improve the collapse of the lesion. In cases where the pneumoperitoneum is employed as an independent procedure, its duration should be approximately equal to that of the pneumothorax.—*El neumoperitoneo en la tuberculosis pulmonar, R. C. Cohen, Hoja tisiol., March, 1946, 6: 48.*—(*L. Molnar*)

Pneumoperitoneum. — Pneumoperitoneum was used in 50 cases of pulmonary tuberculosis. In all but one case, preliminary phrenic paralysis was induced. The average additional rise of the diaphragm was 6.5 cm. The greater part of the rise took place in the first few weeks; after this the diaphgram slowly ascended, reaching the maximum in two to six months. The anterior portion of the diaphragm was found to be higher than the posterior. At induction 1,000 cc. of air were given. Refills of 500 to 1,000 cc. were given twice weekly at first. Each patient complained of pain in the shoulder area. Loss of weight unrelated to other causes was noted in most cases. Dysmenorrhea, small peritoneal effusions and bouts of vomiting were each seen in a few cases. The results were judged "successful" in only 5 cases, and there was improvement in 20 more. It is believed that these poor results are probably due to too ambitious a selection of cases. The location of the lesion was of little importance. The chief factors favoring successful collapse appeared to be: (*1*) pres-

ence of "soft" lesions of recent type and (*2*) absence of extensive adhesions. The presence of a pneumothorax did not improve the chances of successful collapse if unfavorable factors were present. Basal cavities were inconstant in their response to this type of therapy. It was believed that endobronchial tuberculosis was an important factor. The authors concluded that in cases where the lesion can be expected to benefit from a rise in the diaphragm, additional benefit will be derived from a reinforcing pneumoperitoneum. In successful cases, the treatment should be maintained for the same length of time as in artificial pneumothorax.—*Pneumoperitoneum in Pulmonary Tuberculosis, P. W. Edwards & J. Logan, Tubercle, January–February, 1945, 26: 1.—(A. G. Cohen)*

Pneumoperitoneum against Hemoptysis.—Severe hemoptysis in 2 cases of pulmonary tuberculosis was controlled promptly by the induction of pneumoperitoneum. This is preferred to pneumothorax because: (*1*) it is rarely impossible to induce pneumoperitoneum; (*2*) there are fewer hazards; (*3*) it is unnecessary to know which lung is bleeding; and (*4*) an extensive collapse is not required.—*Artifical Pneumoperitoneum as an Emergency Measure in Severe Hemoptysis, A. J. Benatt, Lancet, August 17, 1946, 2: 234.—(A. G. Cohen)*

Electrocardiogram in Pneumoperitoneum.—The treatment of pulmonary tuberculosis with pneumoperitoneum offers the opportunity of studying the cardiovascular changes in the presence of a markedly raised diaphragm. No cardiovascular distress has been observed with this kind of treatment, even if one diaphragm rises as high as the second rib anteriorly. The vital capacity was measured in a number of patients; after months of treatment with pneumoperitoneum refills of 1,000 or 1,400 cc. of air, some of them showed no change at all, others showed a slight increase, and some showed a decrease. The normal electrocardiogram develops the Q_3T_3 pattern and the S-T deflection in lead II becomes flattened. No signs of coronary thrombosis or pulmonary embolism have been noted. The pattern is reversible and becomes normal again with the descent of the diaphragm. A study of the QRS vector and of the ventricular gradient demonstrates that the change of the electrocardiographic pattern is due in the main to a rotation of the heart around an essentially horizontal axis lying in the sagittal plane, the rotation to be described as anticlockwise, as one looks from front to back, that is, the apex moves upward toward the left. This accounts for the often striking distortion of the heart silhouette in the roentgenogram. The apex sometimes becomes buried in the heart shadow. Measurements of the displacement of the heart on the roentgenogram are therefore not reliable. The conclusion to be drawn from the clinical observations together with the results of investigations of vital capacity and electrocardiogram is that pneumoperitoneum treatment in a tuberculous patient with a normal heart does not entail any changes from the cardiovascular point of view. (Authors' Summary)—*The Electrocardiogram in Pneumoperitoneum, A. J. Benatt & W. F. Berg, Am. Heart J., December, 1945, 30: 579.—(G. C. Leiner)*

Plombage.—Introduction of paraffin into a surgically produced extrapleural space has been used to close cavities effectively after unsuccessful thoracoplasty, at Olive View Sanatorium. The type of case best suited for this type of treatment is the one with the small cavity close to the spine which persists after thoracoplasty, in which revision thoracoplasty is usually unsuccessful. The cavity must be accurately localized by planograms and introduction of a needle over the cavity with fluoroscopic aid such that the plomb may be inserted directly over the cavity. Usually only 25 to 50 g. of paraffin are needed. Regenerated ribs forming a firm chest wall to offer counterpressure to the plomb are necessary to good results in this relatively atraumatic procedure.—*Plombage in the Treat-*

ment of Pulmonary Tuberculosis, L. A. Brewer, California & West. Med., Tuberc. Supp., August, 1946, 65: 28.—(P. Q. Edwards)

Relaxing Thoracoplasty.—The authors have devised a series of small thoracoplasty operations designed to change the rigid thoracic cage into a smaller permanently non-rigid ("relaxed") one. The premises are: (*1*) that bilateral cases of pulmonary tuberculosis are not suitable for a modern thoracoplasty operation, nor those with a tension cavity, nor others "with some other concomitant disease;" (*2*) that lung movements are along four "dominant" lines: "by interrupting the muscles of the superior aperture" (all three scalene muscles), "paralyzing the diaphragm, and doing costectomies along the dominant line, the chest is made static and the lung freed from respiratory trauma;" (*3*) that lungs at some time go through a "contracting or hypotensive phase" when the bronchus may be partially or completely occluded by organic disease or its secretions or by decrease in tonus of the bronchial musculature, with the result that alveolar air is removed by the circulation and lung contraction takes place, and that a permanently relaxed, non-rigid cage will promote contraction during this phase better than a rigid collapsed thoracic cage as produced by the standard thoracoplasty operation. "With these principles in mind an operative procedure was undertaken primarily for those with tension cavities and for patients with extensive disease from apex to base on one side but without giant cavities." The procedure consists of small costectomies, in six or seven stages, with complete removal or periosteum each time to leave a permanently relaxed, non-rigid, bony cage. In the final result the rib cage is "relaxed" by resections as follows: anteriorly, 2 inches of cartilage and rib of upper ribs 1–3; a one inch piece of rib from the 4–6 ribs in nipple line; posteriorly, one inch pieces of ribs 1–7 as well as respective transverse processes; a one inch piece of rib from ribs 7–9 in the posterior axillary line. At the first stage the 3 scalene muscles are divided and the phrenic nerve is (usually) crushed. In some cases the entire first rib is resected. Relaxation cannot be accomplished in less than five small stages. Two weeks are usually allowed between operations. To prevent bone regeneration in areas of resection the periosteum may be removed *in toto* or the tissues treated with 20 per cent formalin. The question of paradoxical motion is not discussed. Thirty-three patients were operated upon and were followed for ten to twenty-four months. Of these, 19 are reported to have "negative" sputum but only 2 had sputum cultures. There were 5 deaths (15 per cent); one of these followed conversion into the standard thoracoplasty operation. Of the 33 patients, 21 were declared to be "not suitable for standard thoracoplasty" but criteria employed in judgement are not given. Authors believe this operation will benefit those types mentioned above, or may be used to prepare others for the standard thoracoplasty operation.—*Relaxing Thoracoplasty, O. C. Brantigan, T. B. Aycock, R. Hoffman & H. J. Welch, J. Thoracic Surg., August, 1945, 14: 287.—(W. M. G. Jones)*

Thoracopneumonolysis.—The technique and indications of Fossati's upper thoracopneumonolysis are described. Under local anesthesia a straight paravertebral incision is made and small portions of the upper three ribs are removed. Sometimes the first rib is left intact. The transverse processes are only removed where cavities exist near the mediastinum or the hilum. A pneumonolysis is started at the level of the third rib and followed until the entire apex containing the cavity is well collapsed. The wound is then packed with gauze and partly closed by interrupted sutures. The gauze-pack is withdrawn gradually every three to six days until the wound is closed by granulation. The time of this postoperative treatment varies from three to six months with a medium of four months. In only one case was a wound infection encountered. In none of the cases which were followed up for a period of five years, did the cavity recur. The indications

for this operation are lesions in the upper segment, especially isolated cavities surrounded by apparently normal parenchyma, and old residual cavities.—*Toraconeumolisis superior, Operacion de Fossati, R. P. Sierra, Rev. de tuberc. d. Uruguay, June, 1945, 13: 294.*—(*W. Swienty*)

Pulmonary Resection in Tuberculosis.—The indications of pulmonary resection are discussed, as well as the advantages and disadvantages of this type of surgery in respect to other surgical methods in the treatment of pulmonary tuberculosis. The technique and the postoperative care are described in detail. The results of 31 cases of pulmonary resection, performed in the Oregon University State Hospital for Tuberculosis, are analyzed. Pneumonectomy was done in 10 cases, in which the resection seemed to be the only remedy; in 4 cases the pneumonectomy followed unsuccessful thoracoplasty. Eight patients died of such complications as acute dissemination, cardiac insufficiency, postoperative hemorrhage, pulmonary edema, spread to the contralateral lung, progression of preëxisting contralateral lesions. In one of the surviving patients bronchial fistula and empyema occurred. Only one case of pneumonectomy was successful after a period of observation of one and a half years. Twenty-one cases of lobectomy were performed with a mortality of 3 cases. The results could be considered as good in 17 cases of lobectomy.—*La reseccion pulmonar por tuberculosis, R. Sampietro, Rev. Asoc. méd. argent., March, 1946, 60: 131.*—(*L. Molnar*)

Tubercle Endotoxoid.—Conclusions are based on extensive clinical trial of endotoxoid in native and colored tuberculous patients. Tubercle endotoxoid vaccine was prepared according to the method of Grasset. It is administered by deep subcutaneous injection starting with 0.01 or 0.05 cc. once or twice weekly. This dose is increased, depending upon reactions, by amounts of 0.05 or 0.1 cc. until 2.0 or 3.0 cc. is reached; the latter quantity is suitable for weekly injection. In cases with extrapulmonary lesions, a more gradual ascent is indicated. Reactions are local, general and focal. Locally, painful swellings may occur; these subside without abscess formation. The general reaction is manifested by fever and headache. The focal reaction is probably hyperemic and is shown by increased moisture, occasional pain and increased sputum. Frank hemoptysis may occur, particularly in the early months of treatment. Endotoxoid is then discontinued until sputum is free of blood and modified dosage is instituted. Repeated blood streaking is no contraindication to subsequent readministration. Patients who respond to endotoxoid show a steady gain in weight. Gradual stabilisation with apyrexia occurs. This is due to absorption of exudation surrounding the tuberculous lesion. The focal hyperemic effect is necessary to obtain such an effect. The underlying lesion becomes clearly defined and thin walled and may diminish in size; at this point, collapse therapy may be instituted. Where there is no exudative allergic inflammation, there is little improvement. A stage may be reached beyond which use of endotoxoid may be harmful. Rapid cavitation and dissemination may occur in minimal tuberculosis. Sputum conversion occurs in a minority of patients and endotoxoid treatment is no substitute for collapse therapy in this regard. Pleural effusion may develop during treatment and a negative sputum may become positive after a small quantity of endotoxoid. The treatment has no effect on tuberculous otitis, laryngitis or enteritis. It may flare up an early tuberculous joint or bone. There is no indication of the amount or stage at which the vaccine should be discontinued; it has been administered for periods up to two years. Frequent X-ray films are necessary to gauge the effect and to note the optimal time for collapse. Continued use in clinics without specific control is not recommended. In action and effect, the vaccine is similar to the tuberculins but it is easier to administer and probably less

toxic. The vaccine is without effect in bronchial tuberculosis and in fibroid disease and it may reactivate a healing focus. It is impossible to forecast any individual response. Endotoxoid therapy is suitable for selected patients and is not satisfactory for general use.—*Tubercle Endotoxoid in Pulmonary Tuberculosis, J. Meyer, Clin. Proc., J. Cape Town Post-Graduate Med. Assn., November, 1945, 4: 499.*—(*H. R. Nayer*)

Penicillin in Pulmonary Resections.—The value of penicillin used intrapleurally as well as intramuscularly is well demonstrated in this report of two comparable groups of pulmonary resections. A group of 20 cases who received penicillin showed a marked reduction in postoperative complications and in period of hospitalization as compared with 28 earlier cases who did not have the benefit of the drug. Both groups comprised cases of bronchiectasis, lung abscess, tuberculosis and tumor in approximately the same proportions. Only 20 to 25 per cent of either group had the benefit of individual ligation technique; while 75 to 80 per cent had "grossly contaminated pleural spaces." Silk technique was used in all. In the earlier series, "closed drainage by water seal system was maintained for approximately two weeks, and then was converted to open drainage usually with a smaller tube." In these cases 40 per cent developed bronchial fistula and 100 per cent an empyema. (Reason for "converting to open drainage" must have been the development of empyema, but this is not clear.) The second group received in addition to the usual sulfa drugs (used "for 2 to 3 days preoperatively and for a week postoperatively") penicillin 10,000 units intramuscularly every three hours for two to three days preoperatively and for three to four days postoperatively, or for a week in infected cases. Penicillin 50,000 units in 10 cc. solution was left in the pleural cavity at operation, and this dose injected daily for the next week, after aspiration of collected pleural fluid, by catheter left in the chest for this purpose the first forty-eight hours, and thereafter by needle thoracocentesis. In the second group of 20 cases only one developed empyema, which was rapidly brought under control by merely continuing the penicillin injections after daily aspiration. In this case the empyemal pocket was small and responded promptly to treatment. Penicillin does not alter the surgical treatment of empyemata which fail to obliterate rapidly with aspiration. A case with gross contamination at operation did not develop empyema at all. The penicillin group had an average hospital stay of only twenty-three days compared to thirty-two for the other group.—*Penicillin in Pulmonary Resection, A. B. Valle & M. L. White, J. Thoracic Surg., December, 1945, 14: 437.*—(*W. M. G. Jones*)

Para-aminosalicylic Acid for Tuberculosis.—Study of more than 50 compounds of salicylic and benzoic acid with respect to their inhibitory effect on the growth of tubercle bacilli has led to the discovery that para-aminosalicylic acid is the most effective one so far investigated. Animal experiments showed that this compound was nontoxic for rats and guinea pigs when given for one to two months in a concentration of 5 per cent in synthetic food. This gave a blood concentration of 3 to 7 mg. per cent. The drug was also given a very limited clinical trial. It was felt that daily treatment of tuberculous thoracoplasty wounds with the drug promoted healing of wounds that had existed for from three to six months. It has also been given by mouth. The desired blood levels can be achieved by giving 10 to 15 g. daily. As far as can be told at this point, the drug seems to be of some use. The usual salicylate effect on sweats with a sudden reduction in temperature has not been observed. Periods of one week's treatment alternate with omission of the drug for a similar period. Report of results must await further observations.—*Para-Aminosalicylic Acid in the Treatment of Tuberculosis, J. Lehman, Lancet, January 5, 1946, 250: 15.*—(*H. Marcus*)

Experimental Chemotherapy.—Factors considered in selecting chemotherapeutic agents are toxicity, absorption, transport and cell penetration. Further diserata are the degree of bacteriostatic effect *in vitro* in the presence of serum, concentration necessary for bacteriostasis and not leukocytolytic and the chronic toxicity effects which must not inhibit the natural defense mechanisms of the host. Several new derivatives of diphenyl-sulfones, sulfoxides and sulfides have been synthesized and tested *in vitro* and *in vivo*. The 2,2′ and the 2,4′ diaminodiphenyl sulfones were less bacteriostatic than the corresponding 4,4′ derivative. The diaminodiphenyl sulfoxides show approximately the same inhibitory effects *in vitro* and *in vivo*, as the corresponding sulfones. The 4-benzylidineamino 4′ aminodiphenyl sulfone shows the same therapeutic effect in animals as the parent compound. The halogenated sulfides inhibited growth of tubercle bacilli *in vitro* in dilutions of 1:800,000, although they were highly toxic and showed no therapeutic effect *in vivo*. The sulfoxides, like the sulfones, were antagonized by p-amino benzoic acid, whereas the halogenated derivatives were not.—*Chemotherapy in Tuberculosis, B. L. Freedlander, California & West. Med., Tuberc. Supp., August, 1946, 65: 20.*—(*P. Q. Edwards*)

Diasone Treatment.—Intravenously infected guinea pigs were treated with a daily oral dose of 4 grains of diasone. The treatment was begun coincident with infection. A definite prolongation of life of the guinea pigs occurred. With intravenous and subcutaneous diasone treatment the effects were not consistent. Further experiments showed that diasone in itself is neither sufficient cidal nor static to exert an influence directly on the tubercle bacilli. It is assumed that the effect is one of temporary alteration in the guinea pig body. The significance of oxygen for the growth of the tubercle bacillus and the importance of changes in oxygen tension on its growth has been known for years. It was noted that oral diasone treatment depresses the oxygen content of the arterial blood in guinea pigs. This effect could not be obtained with sulfadiazine which very rarely causes cyanosis. No alteration of the oxygen content was caused by the diasone treatment of tuberculosis in the rabbit. Blood of human patients showed no change either. The effect of diasone treatment in guinea pigs appears to be directly related to the cyanotic effect on the internal organs. Since human patients did not display an evident anoxemia it is doubtful whether a therapeutic effect for diasone has been attained clinically in man.—*The Use of Diasone for the Treatment of Tuberculosis, H. J. Corper & M. L. Cohn, J. A. M. A., April 21, 1945, 127: 1043.*—(*H. Abeles*)

Pharmacology of Streptomycin.—Because penicillin exerts little effect on gram-negative bacilli, much interest is being focused on other agents, among them, streptomycin which has a high activity *in vivo* against various gram-positive and gram-negative bacteria. Studies were undertaken to determine its behavior in patients, and the possibility of toxemic or side reactions. Two experiments were conducted; one to demonstrate the fate of a single dose, and the other to study the response to multiple doses. In both the streptomycin concentration was evaluated by the plate cup method of Stebbins and Robinson. In 20 persons a single dose of 600,000 units was given intravenously. It was found that the blood level decreased at a more or less uniform rate, but is better maintained than with penicillin, a detectable amount usually being present for six hours. Given subcutaneously in one per cent procain, the maximum blood level is not reached for two to three hours and is never as high as following intravenous injection. In 18 patients suffering from a variety of diseases, 3,000,000 units were given in 5 per cent glucose by continuous intravenous drip. Blood levels varied between 20 and 60 units per cubic centimeter of blood. The principle route of excretion is in the urine, 66 per cent of the amount administered being recovered in the average case. When administered

orally at the rate of 1,000,000 units per day, most of the drug was recovered in the feces, one patient having a fecal concentration of 9,000 units per gram of feces. Only occasionally was any streptomycin found in the blood. Since little transfer of streptomycin occurs between the blood and the lumen of the gastro-intestinal tract in either direction, it would seem wise to treat infections involving both the blood stream and the gastro-intestinal tract by both the oral and parenteral routes. When administered intravenously, subcutaneously or intramuscularly, streptomycin is excreted largely in the urine, only 2 per cent of the drug being found in the feces. Samples taken three hours after injection of 600,000 units averaged 350 units per cubic centimeter of urine. Apparently some is retained or destroyed in the body. Streptomycin appears in most body fluids following parenteral injection. Often in peritoneal fluid streptomycin levels were as high or higher than the blood levels at the corresponding time. It is slower to appear in pleural fluid, but was present in moderately high concentrations. It is present also in bile, ocular fluids, amniotic fluid and fetal blood in lower concentrations. Small amounts appeared in the spinal fluid of healthy persons, but in a single case of *Hemophilus influenzae* meningitis the fluid contained 25 units per cubic centimeter. Immediate toxemic effects such as headache, flushes, transient urticaria and fever are not alarming and can be avoided to a great extent by slowing the rate of administration. No late toxemic effects have been observed.—*Studies on Streptomycin in Man: 1. Absorption, Distribution, Excretion and Toxicity, H. A. Zintel, H. E. Flippin, A. C. Nichols, M. M. Wiley & J. E. Rhoads, Am. J. M. Sc., October, 1945, **210:** 421.*—*(G. F. Mitchell)*

Pharmacology of Streptomycin.—Several reports have appeared which indicate that streptomycin may prove of value in the treatment of infections caused by certain gram-negative, gram positive and acid-fast bacteria. Studies were therefore begun to explore the possible methods of administration of streptomycin and to determine its pharmacological properties. Numerous methods of administering the drug were used. Continuous intravenous drip appears to be the most satisfactory method of maintaining constant blood concentration. As much as 4,000,000 units may be given in this manner per day. Intermittent intravenous administration offers no advantage over the intramuscular or subcutaneous routes. The blood concentration after injection is high at first, but falls off more rapidly than when other intermittent methods are employed. Under most circumstances intramuscular injection is the method of choice. One hundred thousand units may be administered in one cubic centimeter of saline every three hours and reasonable concentrations maintained in the blood. Continuous intramuscular injection may also be employed, the drug being given at the rate of eight to ten drops per minute. The subcutaneous route may also be employed and is probably the most comfortable. Fairly high concentrations can be maintained in the blood of patients receiving one hundred thousand units every three hours. This method has the advantage of not requiring highly trained personnel. Streptomycin has also been administered intrathecally without serious untoward reaction, and antibacterial amounts can be found in the spinal fluid for at least twenty-four hours afterward. When used in a nebulizer, 50,000 units per day have been given without interruption for a period of four weeks, during which time no streptomycin could be found in the blood and very little in the urine. A few patients were given streptomycin orally which resulted in a marked reduction in the number of *E. coli* and other organisms of the feces. It could not be demonstrated in the blood when as much as 500,000 units were given per day, and only small quantities were found in the urine indicating non-absorption of streptomycin by the bowels. No detectable amounts of streptomycin were found in the cerebrospinal fluid of patients receiving 200,000 units in a single dose. However, after large doses were given subcutaneously or intravenously in the

presence of meningitis, concentrations in the cerebrospinal fluid approximated one-fifth of that of the blood serum. When administered prior to delivery, it was found to pass the placental barrier and enter the fetal circulation. The concentration in the umbilical cord varied somewhat depending upon the dose and the time interval. It is also found to be present in bile and, for the short intervals employed, it had no effect upon the liver function. From one-half to three-quarters of the total amount administered is excreted during the first twenty-four hours. Some venous irritation at the site of injection has occurred, but actual thrombosis is rare. Even accidental leakage into subcutaneous tissues produces no significant discomfort. When given subcutaneously or intramuscularly, pain may occur at the site of injection, but is usually of short duration. Reactions do not interfere with the administration of the agent, but the size of the injection should be kept as small as possible. Chills and fever may occur. At times general flushing, not unlike a histamine reaction, has been observed when relatively impure streptomycin was given. Dermatitis and urticaria have also followed use of the agent. Several patients complained of severe pain in the joints and muscles. A few with some of the previously mentioned reactions complained of nausea and sometimes vomited. As much as 150 million units has been administered over a period of forty-two days without evidence of interference with renal function. However, administration is followed at times by evidence of renal irritation. Albuminuria and microscopic hematuria have developed. There is no indication of a permanent interference of renal function following cessation of the substance. Impairment of liver function or any undesirable effect on the hemopoietic system have not been observed. — *Streptomycin: Absorption, Diffusion, Excretion and Toxicity, F. R. Heilman, H. C. Hinshaw, D. R. Nichols & W. E. Herrell, Am. J. M. Sc., November, 1945, 210: 576.*—(*G. F. Mitchell*)

Streptomycin Toxicity.—A sensation of dizziness, lightheadedness or giddiness of varying intensity is described by 23 patients receiving streptomycin therapy for tuberculosis. Disturbed equilibrium when standing in the Romberg position and inability to walk a straight chalk line were also seen in most of these patients in whom uniform bilateral decrease in labyrinthine function was demonstrated by caloric stimulation and turning tests. In 5 of the 23 patients some loss of hearing succeeded the labyrinthine disturbances, usually preceeded by a low pitched, constant, roaring tinnitus. Characteristic low tone nerve deafness was revealed by hearing tests. All of these 5 patients had tuberculous meningitis; postmortem examinations on 2 patients showed that the eighth nerves or their nuclei were involved in the tuberculous process. Hearing did improve, however, when the drug was stopped in several cases. Typically, the labyrinthine disturbances were noted after four to eight weeks of therapy, with some degree of compensation by other senses gradually taking place two to four months after treatment was discontinued. Once the dizziness has been brought about there is little tendency for labyrinthine function to return to normal, even when treatment is suspended promptly. The disease must be of sufficient severity to justify subjection of the patient to an uncomfortable state of imbalance while compensation is taking place. The drug must be stopped or markedly reduced in dosage at the onset of low pitched constant tinnitus if permanent hearing loss is to be avoided. The toxic process probably involves the mechanism of the peripheral portion of the eighth nerve; the picture is clouded by gradual development of bilateral loss of labyrinthine function. This could explain the absence of nystagmus in most cases and the lack of true vertigo.—*Toxic Reaction of Streptomycin on the Eighth Nerve Apparatus, H. A. Brown & H. C. Hinshaw, Proc. Staff Meet., Mayo Clin., September 4, 1946, 21: 347.*—(*P. Q. Edwards*)

Breath Sounds.—Differences in pitch between inspiration and expiration are related to the damping effect of the gradually filling and rapidly emptying peripheral alveoli; dilatation and collapse of the alveoli *per se* play no part in the production of the sound, which results from the vibration of the bronchial tree and the transmission of sound through the aerated lung. In tubular breathing, however, an apt analogy is drawn to vibrating strings, insofar as the alveoli play no part in the production or damping of sounds made wholly by vibrations of a fairly rigid tracheo-bronchial system. High frequency vibration accounts for the pause between inspiration and expiration over consolidated lung areas. Tracheal breathing is heard directly through the thin anterior neck which does not modify the sounds produced by direct tracheal vibrations.—*Pulonary Mechanism for Breath Sounds, C. human, Quart. Bull. Sea View Hosp., pril, 1946, 8: 114.*—(*P. Q. Edwards*)

Demonstration of Tubercle Bacilli in Sputum.—The purpose of this study was to compare the efficiency of the sodium hydroxide digestion method, in which potassium alum is used as an aid in concentrating tubercle bacilli in sputum, with the efficiency of the clorox method and direct smear. Identical specimens of sputum were studied by each of the three methods. The results show that the clorox method gave more efficient results than did the sodium hydroxide-alum method and that both the clorox and the sodium hydroxide-alum method surpass the direct smear for finding acid-fast organisms in sputum. Because of the more complete digestion by the clorox method, the centrifuged sediment from positive specimens usually contained more organisms per given amount of sediment than did those obtained with the sodium hydroxide-alum method. When the clorox method is used, the small cotton swab should be moistened in clear blood serum before transferring the sediment from the tube to the slide.—*Detection of Tubercle Bacilli in Sputum: Application of the NaOH-Alum Method, the Clorox Method, and the Direct Smear, G. M. Cameron & R. Castles, J. Lab. & Clin. Med., March, 1946, 31: 361.*—(*F. G. Petrik*)

Acid-fast Organisms in Gastric Contents.—This investigation was undertaken to determine the incidence of acid-fast organisms in the gastric juice. Specimens were obtained from clinic patients subjected to fractional test meals; none of them were known or suspected to be suffering from tuberculosis. Each specimen was concentrated and smears subjected to routine acid-fast stains. The specimens were also cultured on Loewenstein's medium and injected into guinea pigs. Of 171 specimens examined, 7 showed acid-fast bacilli. None of the 7 showed more than two or three such organisms per slide in a prolonged search. They were mostly of a short and stout shape, unlike true tubercle bacilli. On culture 3 of the 7 specimens gave a growth of saprophytic acid-fast organisms which grew equally well at room temperature and failed to produce tuberculous lesions in a guinea pig. All 7 specimens on guinea pig inoculation had failed to produce any lesions when the animals were killed seven weeks later. Control investigations carried out on 3 open tuberculosis cases showed typical tubercle bacilli present in large or moderate numbers in the resting gastric juice.—*Acid-fast Organisms in Gastric Resting Juice, J. Yates, Brit. M. J., October 20, 1945, 2: 530.*—(*D. H. Cohen*)

Tubercle Bacilli in Gastric Contents.—When specimens of gastric lavage are kept standing without neutralization for one or two days before cultures and guinea pig inoculations are made, the tubercle bacilli are damaged to the extent that only about one third as many of the specimens are found positive as in the same specimens worked-up immediately after they are secured. The damaging factor in gastric juice has not been identified.—*Isolation of Mycobacterium Tuberculosis from Gastric Contents Neutralized after Varying Periods,*

Marian G. Sprick & J. W. Towey, Pub Health Rep., May 3, 1946, 61: 648.—(M Pinner)

Toxic Granulations in Tuberculosis.—This is a preliminary report on the diagnostic and prognostic value of the "granulotoxic quotient" in pulmonary tuberculosis. The nuclear changes following different stimuli are well known. Protoplasmatic changes occur also as a reaction to infection and consist in formation of vacuoles and granulations different from normal. These latter appear as large granulations, stained dark red with the May-Grünwald-Giemsa method. In general the leucocytes containing these granulations are enlarged. The authors distinguish two types of neutrophils: those with normal granulations and those with pathological granulations. The quotient: $\frac{\text{pathological neutrophils}}{\text{normal neutrophils}} \times 100$ is normally 3 or less. The granulotoxic quotient was studied on a series of cases of pulmonary tuberculosis in different stages of evolution and also in connection with different methods of treatment. Parallel to the study of the granulotoxic quotient, the sedimentation of the red blood cells, as well as the nuclear index of the neutrophils were studied; these studies showed that toxic granulations were more abundant in progressive cases or in the presence of complications, while they tended to diminish with favorable development of the lesions or of the complications. The granulotoxic quotient seems to be more reliable in prognosis than Arneth's formula or the nuclear index of Bonsdorf.—*Significacion clinica de las granulaciones toxicas de los neutrofilos en tuberculosis pulmonar, J. S. Azparren & V. P. Juarrero, Rev. españ de tuberc., March, 1946, 15: 171.—(L. Molnar)*

Heparin and Blood Sedimentation.—Wide variance of opinion and of results have been reported in regard to the efficiency of the blood sedimentation rate by the use of heparin as the anticoagulant. In general, it may be said that when the optimum concentration of heparin is used the resultant sedimentation rate is then comparable to the standard Westergren method. However, as the concentration of heparin is increased hemolysis of the erythrocytes may occur and the speed of reaction is thus altered. The use of a heparin solution of one part per thousand parts was found best.—*Heparin and the Blood Sedimentation Reaction, G. Nielsen, Acta med. Scandinav., June 30, 1942, 111: 66.—(E. R. Loftus)*

Miliary Tuberculosis.—Three cases of acute miliary tuberculosis are presented. They had the clinical appearance of a "typhoid state" and 2 of them had no roentgenological evidence of miliary dissemination in the lungs. However, they had not the slow pulse of typhoid fever, nor leukopenia. The total white count varied from 5,000 to 11,500 in one patient, from 3,000 to 10,000 in the second and from 5,600 to 14,200 in the third. The third patient had pathognomonic roentgenological findings and, therefore, presented no diagnostic problem in contrast to the other 2 patients. Diagnosis was made more difficult in the second case by negative tuberculin tests (first and second dose of PPD) and a mildly positive Widal test, whose titre, however, did not increase during the illness. Necropsy showed in all 3 cases, acute caseating tubercles with many tubercle bacilli.—*Acute Disseminated Miliary Tuberculosis, E. N. Packard, M. Clin. North America, March, 1946, 30: 263.—(M. Pinner)*

Miliary Tuberculosis.—A review was made of 4,600 autopsies performed at Boston City Hospital during a five-year period. Cases from the Sanatorium Division and of children below the age of 12 were not included. Some form of tuberculosis was found in 310 cases (1.55 per cent). Among these, there were 63 cases of acute miliary tuberculosis, an incidence of 20.0 per cent. The peak incidence of miliary tuberculosis among adults occurred in the third decade, while in the nonmiliary forms it was in the seventh decade. The diagnosis of acute miliary tuberculosis was made antemortem in 16 of the cases (25 per cent). In most cases, the diagnosis was based on X-ray find-

ings, but in several it was made by evaluation of the clinical findings. A history of exposure to tuberculosis was obtained in 16 per cent and a history of previously active tuberculosis in 26 per cent. Anorexia, weight loss, cough, night sweats, dyspnea, chest pain and hemoptysis occurred in 90, 85, 82, 79, 64, 49 and 15 per cent, respectively. None of these symptoms are distinctive of acute miliary, as contrasted with fibrocaseous pulmonary tuberculosis. Tuberculous meningitis occurred in 7 cases. Physical findings were rarely of much diagnostic assistance. The temperature curves showed no consistently definite form; many were very irregular. Rapid pulse rates, often out of proportion to the temperature, generally were found. Rates of 120 to 160 per minute were common. While increase in the respiratory rate was noted frequently, it was not possible to attach clinical significance to this finding in a given case. The patients were in poor general condition. Miliary tubercles were seen in the ocular fundi in one case. Pulmonary findings consistent with the diagnosis of chronic pulmonary tuberculosis were found in 36 cases. The spleen was reported as palpable in 12 per cent of cases. Pleural effusions were found at autopsy in 19 cases, but were detected clinically in only 5. Pericardial effusions were found at autopsy in 9 cases; in 5 of these the amounts were small. Four cases showed intraperitoneal fluid at autopsy. The hospital course ranged from twelve hours to 225 days. The average length of stay was two to four weeks. Eighty-three per cent of the patients died two months or less after the onset of acute symptoms. Total leucocyte counts ranged from 1,600 to 20,700. There was a leucopenia in 24 cases, leucocytosis in 14 and a normal count in 16. Increased percentages of neutrophils were found in 89 per cent; immature forms were quite frequent. This was as true in cases where leucopenia was present as in the others. Miliary tubercles were found in the bone marrow at autopsy in 33 of 37 cases. Moderate normochromic anemia was found frequently. In 2 cases there was thrombocytopenia in addition to leucopenia. The following requirements were set up for the pathological diagnosis of acute miliary tuberculosis: that the tubercles be acute, provoking little or no fibrous tissue reaction; that the disease be generalized sufficiently to involve the liver, spleen and at least one additional tissue; and that the tubercles conform, with regard to size, to the miliary description. Chronic tuberculous foci were found in 95 per cent. The most numerous organs involved were the lungs, lymph nodes, intestines and genito-urinary tract. The lungs were involved in 71 per cent. The organs most frequently involved by miliary lesions were the spleen, liver, bone marrow, lungs, kidneys and adrenals in the order named.—*Acute Generalized Miliary Tuberculosis in Adults, C. B. Chapman & C. M. Whorton, New England J. Med., August 23, 1946, 235: 239.*—(*A. G. Cohen*)

Tuberculous Meningitis.—This is a report of 3 cases of tuberculous meningitis in young adults, observed at Tilton General Hospital. The first patient, a 27-year old Negro, had disseminated tuberculosis and meningitis with a lymphocytic, leukemoid blood picture (maximum: 80,000 white cells with 99 per cent lymphocytes) in the beginning of his disease, but the total white count dropped to 3,650 with 46 per cent lymphocytes one month before death. The second patient, a 24-year old Negro, had tuberculous meningitis whose initial symptoms suggested a postpneumonic pleural effusion and whose neurological symptoms posed the differential diagnosis of Jacksonian epilepsy. The third patient, a 38-year old white man, had genito-urinary tuberculosis with eventual dissemination to the meninges. It is believed that the meningeal involvement in these 3 cases occurred by hematogenous seeding; an older tuberculous focus could not be found in the brains.—*Tuberculous Meningitis with Unusual Features in Young Adults, H. L. Katz & H. A. Abel, M. Clin. North America, March, 1946, 30: 271.*—(*M. Pinner*)

Tuberculosis from a Cat.—Although several cases have been reported in which tuberculosis

was apparently transmitted from man to cats, this is the first case where a human was undoubtedly infected by a diseased cat. The case history of a 3-year old boy is given. The patient was bitten on the right forearm by a cat which was found dead two days later. The pinpoint cutaneous wounds seemed to heal temporarily, although within a month they had become infiltrated and enlarged with rapid development of axillary adenitis and fever. The tuberculin test was positive (3 mg. of tuberculin). The chest film showed both lung fields to be filled with small dense patches; the patient was acutely ill. Death from tuberculous meningitis occurred three and one half months after the cat bite. An autopsy revealed an ulcerative tuberculosis of the skin of the forearm, caseous adenitis of the right coronoid fossa, right axilla, mediastinum right hilum and superior portion of the abdomen, miliary lesions throughout the lungs, spleen, liver and kidneys and tuberculous meningitis. Guinea pig inoculations and cultures were positive for tubercle bacilli of the bovine type.—*The Transmission of Tuberculosis from Cats to Human Beings: Report of a Case, J. Lewis-Jonsson, Acta tuberc. Scandinav., 1946, 20: 102.*—(*P. Q. Edwards*)

Tuberculous Rheumatism.—This condition, although rare, has been reported from time to time. It may be diagnosed if rheumatic phenomena precede by a short interval, or accompany, an active tuberculous infection. According to Poncet and Leriche, three clinical types may be recognized: (*1*) arthralgia; (*2*) acute rheumatism, often with pericarditis; and (*3*) chronic rheumatism. Tuberculous rheumatism is usually milder than the joint manifestations of rheumatic fever. The pain and swelling are less, the temperature usually not high and the response to salicylates is often lacking. Except in the chronic type, the joint manifestations subside quickly. The author reports 6 cases in which the time relationship and the further development justifies a diagnosis of tuberculous rheumatism. All 6 children developed frank tuberculosis, and 2 children died of this disease. No attempt was made in this series to recover tubercle bacilli from the affected joints, and the author doubts that this could be accomplished. He regards tuberculous rheumatism as an expression of altered immune mechanisms in a susceptible host in the sense that Coburn has expressed himself on rheumatic fever.—*Tuberculous Rheumatism, W. Sheldon, Lancet, January 26, 1946, 250: 119.*—(*H. Marcus*)

Pleural Effusions.—So-called idiopathic effusions are considered to be tuberculous unless proven otherwise. The theoretically possible mechanism of their pathogenesis are discussed. A group of 59 patients with effusions were thoroughly studied. Their clinical course and roentgenological appearance are described. Pertinent data, not generally known, are presented along with the usual findings. White blood counts and differential counts were within normal limits in all phases of the disease, but slight leucocytosis occurred in some cases in the early phase. In a high percentage of patients, the sedimentation rate was significantly increased. All but one patient reacted to tuberculin. Throat cultures, made in 36 patients, yielded *S. viridans* and *S. hemolyticus* but these bacteriological findings showed no correlation with the clinical course. The titre of cold agglutinins was not increased in 23 patients so examined. No persistent elevation of the antistreptolysin titre was found in 23 patients. The specific gravity of the effusion was always above 1.015; protein varied between 3.5 and 6 mg. per cent, and the albumin-globulin ratios were similar to those in the plasma. Cell counts of pleural fluids varied from 100 to 3,000; lymphocytes usually predominated. No secondary infection was found in any specimen. Tubercle bacilli were demonstrated by culture and guinea pig inoculation in 5 out of 21 patients. In sputa and gastric contents, tubercle bacilli were found in 5 patients Fluid was withdrawn only for laboratory studies or if indicated by pressure symptoms or if it did not resorb within eight weeks of onset. However, it is thought preferable to evacuate all fluid following the acute initial phase in order to prevent pleural

thickening with its impairment of respiratory function. It is also advised to induce a small pneumothorax in the hope of preventing pleural obliteration.—*Tuberculous Pleural Effusions, D. J. Feldman & H. P. Lewis, M. Clin. North America, March, 1946, 30: 245.*—(*M. Pinner*)

Prognosis in Pleural Effusions.—Tuberculous pleurisy may be cured without apparent anatomical sequelae, but most often different degrees of permanent changes result after the clinical cure of the pleurisy. Pleural thickening, pleural adhesions, complete symphysis of the pleural cavity and sometimes extensive fibrosis of the pleura and of the lung, fibrothorax, represent conditions having a great potential importance on the future of the patient. There is sufficient evidence to contradict the current belief that pneumothorax leads necessarily to pleural symphysis. Pneumothorax could be re-initiated after having reëxpanded the lung, even if the course of the treatment had been complicated by pleurisy. It is also certain that pneumothorax can be obtained occasionally in patients who had previously had an exudative pleurisy. Other observations referring to the enlargement of the pneumothorax pocket after a traumatic perforation of the lung, or as a consequence of the development of abundant pleural fluid, speak in favor of the possibility that certain types of adhesions can be broken. The anatomical sequelae of pleurisy cannot be considered as true scars: they have to be regarded rather as residual tuberculous lesions with the ever present possibility of a reactivation due to the possible persistence of virulent tubercle bacilli and of tuberculous granulations. Pulmonary involvement may also follow persistent tuberculous foci in residual pleural lesions. Tuberculous changes in the fascial layer, surrounding the parietal pleura, may also represent potential foci for further evolution and spread.—*Del pronostico a largo plazo en la pleuritis tuberculosa, R. G. Juarez & D. Oraindi, Rev. españ. de tuberc., May, 1946, 15: 331.*—(*L. Molnar*)

Bilateral Pleural Effusions.—In the course of six and a half years, during which time 2,012 patients were admitted, there were 6 cases of bilateral tuberculous pleural effusion. Five of the cases developed evidence of disseminated tuberculosis by X-ray. Generally, during the stage of resolution of the first effusion, an effusion appeared on the opposite side, followed later by the appearance of miliary tubercles. It is believed that the effusions are due to hematogenous invasion of the pleura. The prognosis is grave. In this series, 4 of the 5 patients developed a tuberculous lesion of the spine and died.—*Bilateral Tuberculous Pleural Effusions, H. P. Fernandes, Tubercle, September–October, 1944, 25: 82.*—(*A. G. Cohen*)

Radiology of Pleural Effusions.—The typical roentgenogram in cases of pleural effusion is quite familiar. According to Kaufnitz such pleural effusions may be divided into three regions, the lowest and most radiopaque consisting almost entirely of fluid, the middle or translucent area due to a moderate amount of fluid slightly compressing the lung, and the uppermost representing a film of fluid that is too thin to be seen in the X-ray film. According to Ganter, effusions of less than 400 cc. cannot be demonstrated by physical examination or ordinary chest X-ray films. Rigler has shown that all pleural transudates and most pleural exudates shift with change in position of the patient. Therefore, by placing the patient in a variety of positions one can detect small effusions and differentiate thickened pleura from fluid. Thus, when a patient is supine, the characteristic appearance of fluid is no longer present and the involved hemithorax becomes cloudy, but with the patient in the lateral decubitus position a hazy shadow occupying the costophrenic angle may be seen. The Trendelenburg position is also of value, the fluid shifting to the upper part of the hemithorax. When there is no change in the position of the fluid, it is usually a purulent exudate or a nonpurulent exudate of long standing allowing the formation of adhesions and partial encapsulation. The concavity of

the upper margin of the pleural fluid is due to a combination of forces which include hydrostatic pressure, the relative rigidity and fixation of the hilar region, the normal subatmospheric intrapleural pressure which is maintained by the elastic retractility of the lung, the cohesive force existing between the pleural surfaces with resultant capillarity and the character of the fluid. The authors are concerned here with free fluid in the absence of pneumothorax in which the appearance is atypical. Even in the absence of air the upper surface of a pleural effusion may be flat or even convex. This is often seen in exudates with a high specific gravity and protein content. When the fluid surface is convex, simulating elevation of the diaphragm or subdiaphragmatic abscess, X-ray diagnosis may be difficult. In the authors' experience the most common atypical pleural effusion is that in which fluid accumulates in the paramediastinal pleural space. This may assume a variety of appearances. An anterior paramediastinal effusion is seen as an opacity having a well defined margin parallel with the right or left cardiac border, and this type of effusion is often surprisingly large in volume and is often described as ribbon-shaped. Posterior paramediastinal effusions present ribbon-shaped shadows running parallel to the right or left borders of the vertebral column or triangular opacities with the base resting upon the diaphragm and the apex directed toward the hilum. Physical signs may be absent, but when the effusion extends to the chest wall, the signs of pleural effusion are present lateral to the vertebral column. In most cases the heart and adjacent paramediastinal fluid are of different densities, but at times they are almost identically opaque, and it may be difficult to determine where the lateral border of the heart ends and the effusion begins. Oblique and lateral views, combined with fluoroscopic examination, will disclose the nature of the process. All of the cases of mediastinal effusions in the authors' series were of tuberculous origin. Clinical recognition of fluid in the interlobar spaces is difficult. A thorough knowledge of the anatomical location and the roentgenological appearance of the interlobar fissures is important in the evaluation of this type of effusion. At times the presence of the effusion in the interlobar fissures can be seen only when the patient is placed in certain positions. The short interlobar fissure is more commonly the site of interlobar effusions than the long fissures. When only a small amount of fluid is present in the pleural cavity, it does not rise as high as the short fissure with the patient erect, but when the horizontal position is assumed, the fluid reaches a higher point and may be drawn into one of the interlobar fissures by the force of the capillarity existing there. This is even more likely in the lateral decubitus position. When the effusion is large enough, the fluid reaches and enters the interlobar fissure even when the patient is upright. The X-ray appearance of the interlobar portion of the effusion is determined by the course of the interlobar fissure and the size of the effusion, small ones being narrow and band shaped while large ones are ovoid. This type of interlobar effusion is more common in effusions of tuberculous or pneumonic origin, but may be seen occasionally in cases of congestive heart failure. Many reasons are offered for the unusual appearance of atypical pleural effusions, but any factor altering the factors accompanying the ordinary effusion will affect the contour of the fluid, though it must be admitted that in some cases there is no satisfactory explanation.—*Unusual Pleural Effusions, S. Katz & H. R. Reed, Radiology, August, 1945, 45: 147.*—(*G. F. Mitchell*)

Treatment of Tuberculous Empyema.—Since promanide was found to be useful in the treatment of tuberculous abcesses, it was decided to try it in tuberculous empyema. A preparation was obtained which, when diluted 1 to 7 in sterile water, gave a 5 per cent solution of promanide in 1:1,000 phemeride. The latter compound is an organic detergent or wetting agent. Four cases were treated; 2 of these had mixed infections. After each aspiration of pus, 8 cc. of the solution were injected. This was done every one to three

weeks. In all cases, there was progressive thinning of the pus which eventually became clear and serous. In all cases the lung re-expanded with resulting obliteration of the pleural space. It is believed that the untoward reactions noted in previously reported cases were due to too large amounts of promanide.—*Treatment of Tuberculous Empyema by Aspiration followed by Instillation of Promanide with Phemeride, T. F. Jarman & G. J. Morris, Tubercle, May-June, 1945, 26: 85.—(A. G. Cohen)*

Tuberculosis of Serous Membranes.—The influence of living conditions on the forms and course of tuberculosis was studied on the basis of 456 cases of tuberculosis of the serous membranes. These patients belonged to two very different categories: 441 were repatriated prisoners, and 15 came from a very privileged and homogeneous collectivity of the Paris zone, among whom physical and mental strain had not essentially increased during the war and whose food rations had remained very superior to those of the general population. This group consisted of healthy males between the ages of 19 and 40. The 441 cases of repatriated prisoners could be divided as follows: 320 cases of simple sero-fibrinous pleurisy, 21 cases of peritonitis, 100 cases of polyserositis with a combination of pleural, peritoneal, and pericardial involvement. Ten cases were followed by meningitis. After analysis of these cases the following conclusions are drawn: (*1*) There is a high incidence of tuberculosis of the serous membranes in the adult at the present time. (*2*) High incidence of pleurisies with protracted course (lasting longer than three months). (*3*) High incidence of cases with polyserositis, with an unusually high number of peritonitis, pericarditis and meningitis in the adult. (*4*) High incidence of relapses (33 per cent), often after a prolonged interval of apparent good health (three months to one year). Repeated relapses were observed in 30 cases. In contradistinction to these findings among the repatriated prisoners of war, the cases of the second group showed no peritoneal, pericardial or meningeal involvement, the only serous membrane involved being the pleura. The incidence of relapses was only 12 per cent as compared to 33 per cent in the first group. The average duration of the pleurisies was less than three months.—*Étude sur les formes actuelles de la tuberculose des séreuses chez l'adulte: Influence des conditions de vie, Bariety & Barrabe, Recueil des travaux Inst. Nat. d'hyg., 1944, 1: 214.—(V. Leites)*

Pleural Calcifications.—The past history, the etiology and diagnosis and the evolution of 38 cases of pleural calcifications were studied. In 12 cases there was trauma to the chest in the past history; exudative pleurisy was recorded in 11 cases; in 9 cases such pleuropulmonary illnesses were noted as tuberculosis, bronchitis, pleurisy and asthma. The extension of the calcifications varied from 4 cm. to a complete involvement of the pleura. The most extensive pleural calcifications occur after injury to the chest. The age of the patients was most often from 40 to 60, but there were some cases in other age groups. In more than one half of the patients the pleural calcifications represented unexpected findings on routine chest X-ray films. In other cases there were some signs and symptoms, pointing toward the pleura. In 2 cases stabbing pain and a history of trauma have led to the suspicion of pleural calcifications and were confirmed by X-ray examination.—*Consideraciones que sugiere el estudio de 38 cases de calcificaciones pleurales, O. F. Noguera & G. Gotta, Rev. Asoc. méd. argent., March, 1946, 60: 138.—(L. Molnar)*

Perforating Tuberculous Tracheobronchial Lymph Nodes.—The postmortem examination of a 3-year old boy is reported, who contracted tuberculous infection from his father at the approximate age of one year. The clinical course was characterized by asthma-like attacks of paroxysmal cough, successively becoming more severe, until the last attack terminated in death. There was a primary focus in the subpleural region of the right

upper lobe and paratracheal adenopathy on the same side which later invaded the intertracheobronchial and the paratracheal groups of the opposite side. The asthma-like attacks were due to the compression of the tracheobronchial tree by the intertracheobronchial lymph nodes. Eventually a perforation of the bronchial wall occured and at the successive paroxysms caseous material was aspirated in different portions of the lung causing areas of apneumatosis. Some of these underwent a process of carnification. In the terminal phase a wide perforation occurred in the trachea followed by a complete occlusion of both stem bronchi. The clinical symptomatology as well as the postmortem findings in this case correspond to the interpretation more widely accepted nowadays, that the pulmonary findings associated with tracheobronchial adenopathy are represented by areas of apneumatosis rather than by "epituberculous" infiltration. The description of this case is preceded by an outline of the clinical and pathological pictures in the various phases of perforating tracheobronchial adenopathy, reviewing also the most recent literature concerning this problem.—*La evolucion perforativa tracheobronquial de la adenopatia caseosa primaria, J. J. Scandoglio, Hoja tisiol., December, 1945, 5: 421.*—(*L. Molnar*)

Tuberculous Lymph Nodes.—Four cases of tuberculous cervical adenitis and one of tuberculosis of the sternum were treated by the administration of 50,000 units of calciferol twice daily. This resulted in marked improvement in 4 of the cases.—*Tuberculous Glands and Sinuses Treated with Calciferol, H. J. Wallace, Lancet, July 20, 1946, 2: 88.*—(*A. G. Cohen*)

Tuberculous Lymph Nodes.—Four forms are distinguished: (*1*) Hyperplastic form (without caseation). (*2*) Fibro-sclerotic form with marked development of fibrous tissue and sometimes calcification. Small caseous foci are present, but well encapsulated. (*3*) Caseous form: caseation occupies often the whole parenchyma of one node. In most of these cases there is liquefaction, perforation and fistula formation. (*4*) Fibro-caseous form with marked fibrous periadenitis and caseous foci of varying degree. Three hundred eighty patients with tuberculous adenopathies were followed in the course of nine years. The fatality was 3.7 per cent. The basis of treatment was sanatorium care. The most effective methods of active therapy were considered to be a combination of heliotherapy, ultraviolet radiation and tuberculin. Treatment with tuberculin alone produced a standstill of the process in 58.3 per cent, of cases, ultraviolet alone in 43.2 per cent, combined heliotherapy and ultra-violet in 62 per cent. Heliotherapy was applied as a course of 30 to 40 sessions. The duration of each session was increased gradually from five to fifty to sixty minutes. Heliotherapy was considered as contraindicated: (*1*) during the initial period of development of a tuberculous adenopathy, and during periods of exacerbation; (*2*) in the presence of an active primary focus in the lung or an infiltrative process around the hilar nodes; (*3*) in cases with marked enlargement of the hilar and paratracheal nodes on the X-ray film, suggestive of caseation; (*4*) in cases with general lymphatic involvement, marked toxemia, kidney involvement and amyloid. According to the authors treatment with tuberculin is indicated in the hyperplastic forms as well as in the caseous and fibro-caseous forms of adenopathy. It is contraindicated in (*1*) universal involvement of the lymphatic system, (*2*) in the presence of active primary lung lesions, (*3*) during an exacerbation of a tuberculous process anywhere in the body. The application of tuberculin treatment is useless in extensive fibrosis of the lymph nodes. The dosage is dependent on the individual sensitivity. Marked focal and general reactions are to be avoided. In 70 cases tuberculin was given through the intranasal route, beginning with one drop of Koch's Old Tuberculin (0.05 cc.). The course was terminated in most cases with 15 drops (0.8 cc.). The course of treatment

was repeated after four to six weeks. With this method the children tolerated large doses of tuberculin without inconvenience. The tuberculous process was arrested in 58.3 per cent of cases, improved in 28.9 per cent and not influenced in 10 per cent; 2.8 per cent of the cases became worse with marked focal reactions, general downhill course, fever and weight loss. Exudative pleurisy developed in one case.—*Tuberculous Lymphadenopathy, I. N. Osipov & A. S. Soboleva, Probl. tuberk., 1945, 4: 5.*—(*V. Leites*)

Tuberculous Cervical Lymph Nodes.—Excision of tuberculous lymph nodes of the neck has fallen into disrepute of late. In the author's experience, however, there is still a definite indication for operative removal. He has performed this operation on 25 patients, 24 of whom he was able to follow for from one to eight years. Twenty-one patients have remained well. Three patients had recurrences, one on the contralateral side. Of these 3 patients, 2 were cured after another operation, and one after two more operations, including tonsillectomy. Patients must be carefully selected for operation. They must be free of active tuberculous foci elsewhere in the body, and the local process must be at a complete standstill. There must be evidence that no new groups of nodes are becoming involved, which means that the process must have been under observation for some time, or an adequate history of an unchanged condition for some time must be obtained. The patients must be vigorous and in good condition. The presence of fistulous tracts or abscess formation is no contraindication. The operation is lengthy and difficult, inasmuch as the nodes are often adherent to the great vessels and nerves of the neck. No complications were observed, and in the majority of cases the wound healed by primary intention. Only in 3 cases a small drainage tract remained, which closed after two weeks. The operation is advised when conservative treatment, especially sanatorium treatment, has failed. It seems advisable to coördinate the operation with sanatorium treatment, although this is not a necessity. The pathogenesis of the tuberculous adenitis is not always clear. The primary focus is presumably in the oral, nasal or pharyngeal cavity in the majority of cases, but this cannot often be demonstrated. Sometimes neck nodes become involved in an ascending fashion from tracheobronchial nodes. These cases offer less favorable scope for operation, inasmuch as the source of the infection, the mediastinal nodes, must be left behind.—*Die operative Behandlung tuberkulöser Halslymphome, E. Kaiser, Schweiz. med. Wchnschr., March 2, 1946, 76: 165.*—(*H. Marcus*)

Tuberculosis of Nasal Septum.—Two cases of tuberculosis of the nasal septum were observed. The first observation concerned a young male with cavitary disease. The second case was that of an elderly woman with healed Pott's disease and residual pulmonary changes. Histological examination corroborated the diagnosis of tuberculosis in both cases. The different pathogenetic possibilities are discussed without reaching a definite conclusion in either case. Chronic pulmonary tuberculosis is frequently associated with atrophic rhinitis which constitutes a debilitated area susceptible to infections. Radium therapy followed by electro-coagulation improved markedly the lesions observed in the first case, while tuberculin and gold treatment associated with radium and Finsen therapy completely cured the granuloma in the second case.—*Tuberculosis del septum nasal, A. M. Calafat, Hispalis méd. (Sevilla), November, 1945, 17: 5.*—(*L. Molnar*)

Promin against Tuberculous Laryngitis.—The cases treated suffered from all types and degrees of pulmonary tuberculosis. Only those with ulcerative or granulomatous laryngitis were selected. A solution of 20 per cent promin in 50 per cent glycerine was sprayed into the throat with the tongue held extended. Two to four puffs were given every day. A preliminary routine of silence for two to four weeks was carried out. Alter-

nate cases were sprayed with warm chaulmoogra oil. In all, 28 patients were treated, of whom 14 received promin, 12 chaulmoogra oil and 2 promin and the oil. There was no improvement in any case unless the pulmonary condition improved. The earliest cures were achieved in four weeks with the oil and seven weeks with promin. The average cure came in three months with each drug. The end results were, in general, disappointing but the lesions did appear cleaner. Of the promin cases, 7 out of 14 showed marked improvement, 3 were not benefited and 2 grew worse. Of the chaulmoogra oil cases, 5 were cured, 6 not benefited and one grew worse. The possibility that the enforced silence during the period of treatment may have been a factor in improvement must be considered. It was concluded that promin is not more efficacious than chaulmoogra oil, but that it is worth trying until something better is found. At present, the author is giving three treatments a day, with better results.—*Treatment of Tuberculous Laryngitis with Promin (Promanide), I. G. Robin, Tubercle, November-December, 1945, 26: 186.*—(*A. G. Cohen*)

Tuberculous Osteoarthritis.—Active osteoarticular tuberculosis in children with high sedimentation rate seemed in the past to represent a definite contraindication to surgery. Various surgical interventions were performed, however, in 18 cases of osteoarticular tuberculosis with sedimentation rates ranging from 30 to 110 mm. per hour, during the last five years. In none of these cases was an exacerbation of the lesions observed during a period of over ten months. Only one child died two years after the intervention as a consequence of amyloidosis following new localizations occurring one year postoperatively. The experience of this author shows that the only definite contraindication to surgery is the association of active pulmonary tuberculosis with the osteoarticular involvement.—*Oportunidad del tratamiento quirurgico de la tuberculosis osea en el niño, P. R. Grove, Rev. méd. de Chile, April, 1946, 74: 290.*—(*L. Molnar*)

Renal Tuberculosis.—Because of generalized sensitization during the first invasion by tubercle bacilli, when bacilli are present in glomeruli of a sensitized kidney they are arrested by exudate and local inflammation and produce tuberculous changes long before their appearance in the urine. Renal tuberculosis, then, is a separate pathological entity; tuberculous bacilluria is always an indication of a caseous or ulcerative tuberculous lesion of the kidney. Five modes of infection are possible: (*1*) primary, through the anterior urethra; (*2*) ascending from the genital organs; (*3*) direct extension; (*4*) lymphatic or (*5*) hematogenous. The last named is undoubtedly the most common source of spread, as evidenced by the high percentage of bilateral renal disease as well as the largely cortical and cortico-medullary distribution of lesions within the kidney. Healing of small nodular lesions and ulcers may take place spontaneously in a very small percentage of patients. Post-nephrectomy breakdown of the remaining kidney is such a real hazard that careful evaluation, both medical and urological, of the patient's tuberculous involvement must precede any surgery. Prognosis should be guarded for eighteen months after removal of one kidney, as early breakdown of the contralateral organ is the rule in the majority of cases.—*Pathogenesis and Prognosis of Renal Tuberculosis, A. Sporer, Quart. Bull. Sea View Hosp., April, 1946, 8: 120.*—(*P. Q. Edwards*)

Renal Tuberculosis.—In a series of 240 nephrectomies for tuberculosis, guinea pig inoculation was done in 65 cases with urine from the supposedly healthy kidney. In 18 out of 65 cases, positive results were obtained. The author feels that the mere demonstration ob tubercle bacilli from the "healthy" kidney need not deter from the proposed nephrectomy, provided function and contrast vizualization are normal, and provided that no pus and a minimal amount of albumen

are found in the urine. Of the 18 cases who had positive tests from their "good" kidney, 10 recovered completely following nephrectomy even to the extent that guinea pig inoculation from the remaining kidney became negative and preëxisting bladder tuberculosis healed entirely. The remaining 8 cases fared less well. Tubercle bacilli may be carried into the pelvis of the healthy kidney by instruments during cystoscopy, and thus give a positive animal test. Another possibility is that well circumscribed parenchymal lesions occasionally involve a papilla and a small number of tubercle bacilli may be carried into the urine. Such lesions may heal spontaneously or continue to exist in an encapsulated well circumscribed nonprogressive form. When tubercle bacilli are demonstrated from a kidney without microscopic urinary findings and without definite X-ray evidence of renal tuberculosis, it is well to defer considerations of nephrectomy until it becomes clear that the hematogenous seeding has stopped. During the course of observation, a better decision can be made as to which kidney is more involved and in need of removal. On the other hand, if one kidney is grossly involved when the patient is first observed, it is best to proceed to nephrectomy regardless of the bacteriological findings from the "healthy" kidney.—*Die Feststellung der Gesundheit der einen Niere bei der Nierentuberkulose, F. Suter, Schweiz. med. Wchnschr., February 16, 1946, 76: 125.*—(*H. Marcus*)

Streptomycin in Urinary Tract Tuberculosis.—Twelve patients with genito-urinary tuberculosis were treated with streptomycin. Eight of these patients had tuberculous cystitis with tuberculosis in the solitary kidney, the other kidney having been removed previously because of tuberculosis. The remaining 4 patients had bilateral renal tuberculosis and tuberculous cystitis. Streptomycin was given intramuscularly, every three or four hours, in daily doses of at least one gram for a minimum of thirty-one days. Results of treatment are evaluated under several headings: (*1*) clinical symptoms, such as dysuria, pain, frequency and nocturia, in which 6 patients noted marked improvement; (*2*) cystoscopic examination, which showed definite improvement in the appearance of the bladder in 4 cases; (*3*) the degree of pyuria, showing decrease in 8 patients; (*4*) staining urinary sediment for tubercle bacilli, a procedure of equivocal value because of technical difficulties; (*5*) culture and guinea pig inoculation for tubercle bacilli, 2 cases turned negative during treatment; and (*6*) pathological examination of 2 surgically excised kidneys and one autopsy specimen in which reparative processes were noted in one of the 3 specimens. Streptomycin is not a substitute for surgical treatment where such is feasible in genito-urinary tuberculosis, although encouraging results are obtained in the few inoperative cases in which the drug has been used recently.—*Streptomycin in the Treatment of Tuberculosis of the Urinary Tract, E. Cook, L. Greene & H. Hinshaw, Proc. Staff Meet., Mayo Clin., July 24, 1946, 21: 277.*—(*P. Q. Edwards*)

Tuberculosis of Mamma.—One case of tuberculosis of the mammary gland, associated with caseous axillary lymphadenopathy is described. The axillary lymphadenopathy constituted a polylobulated mass of broken down lymph nodes with central calcification and with relative integrity of the periphery. The mammary gland contained a small caseous nodule surrounded by tuberculous granulation tissue. The patient had had a long-standing pulmonary tuberculosis and the mammary lesion appeared after a delivery. The tuberculosis in the mammary gland was secondary to the axillary lymph node tuberculosis, which, in its turn, followed the pulmonary localization. Tuberculosis is rarely localized in the mammary gland. The infection of the mammary gland may occur through the canalicular system, through the lymphatic system or it may be hematogenous in origin. The canalicular infection would represent the only primary form of mammary tuberculosis, but it is uncertain

whether it exists. The ascending lymphatic origin with a point of departure from the skin or from the nipple is also problematic. The lymphatic connections between the axillary chain and the drainage system of the mammary gland constitute the basis on which the author admits a retrograde lymphatic origin of the mammary tuberculosis from the axillary lymph node tuberculosis.—*Tuberculosis de la glandula mamaria, I. I. Scandroglio, Hoja tisiol., September, 1945, 5: 320.*—(*L. Molnar*)

Growth of Tubercle Bacilli in Liquid Media.—Virulent tubercle bacilli are able to yield an abundant growth in simple synthetic media by synthesizing their structural and metabolic constituents from a few mineral salts and organic compounds. But it is often difficult to initiate the growth of small inocula on such media and, when growth develops, the bacilli multiply extremely slowly. As a result of this slow growth the cells present in these cultures vary greatly in age and therefore in physiological state. Heterogeneity of the cell population is further increased by the formation of pellicles or clumps, the environmental conditions prevailing in the centre of these masses differing greatly from those prevailing at the periphery. It has been shown that a two-week old culture of human tubercle bacilli contains a very large proportion of dead cells and it is likely that many of these have undergone varying degrees of autolysis. Investigations are in the course of being reported having to do with the factors which affect the initiation, rate and mode of growth of tubercle bacilli. The present paper is limited to a consideration of the effect of certain substances on the initiation of growth of small inocula and on the state of dispersion of the cultures developing in liquid media. A basal synthetic liquid medium was employed, of simple composition (modified Kirchner medium). To this the different test substances could be added and the effects on the growth noted, the unaltered medium serving as a control. This basic medium consisted of asparagine or hydrolysate of casein (the nitrogen source) plus sodium citrate and magnesium sulphate, all dissolved in a phosphate buffer. Chiefly human and avian strains were used in the experiments, and for inoculation these were suspended in a 0.2 per cent yeast autolysate with or without a small amount of glucose. The addition of the yeast adds water-soluble vitamins to the medium, which may or may not add to the efficiency of the latter. Previous investigations have shown that certain synthetic water-soluble lipids exert a favorable effect on the growth of tubercle bacilli. These lipids consist of esters of long chain fatty acids and act mainly as wetting agents. Of these an ester of oleic acid (sorbitan monoöleate, "Tween 80") proved most satisfactory in promoting submerged and diffuse growth of mycobacteria throughout the depth of synthetic liquid media. The addition of the oleic acid ester to the control medium changed the character of the growth from one consisting of large compact granules to one in which isolated cells and microscopic loose clumps prevailed. The bacilli constituting this more dispersed growth were typical in morphology and acid-fastness, although the growth took place throughout the medium and was not limited to its surface. The addition of glycerol to the base medium in small amount (0.5 per cent) did not materially affect the growth of bacilli. In 5 per cent amount it showed definite inhibitory effect, the least with the purest glycerol (redistilled). With C.P. glycerol no growth was obtained. Glycerol "reagent" gave intermediate results. It is apparent that certain samples of glycerine (C.P. grade) contain impurities which are toxic for the tubercle bacillus when added in a concentration of 5 per cent to the basic medium. Some of this inhibitory effect may be due to physical factors, since toxicity was also observed when glucose or mannitol in a final concentration of 5 per cent was substituted for glycerol. When administered in small amounts (0.5 per cent) unheated glucose definitely enhanced the growth of the bacilli. It is

known that purified serum albumen facilitates the submerged growth of tubercle bacilli in synthetic liquid media. In one series of cultures, this material in the form of a desiccated product (bovine serum albumen fraction V), was added to the basic medium, with and without the presence of "Tween 80". It was found that albumen alone facilitated the initiation of growth of small inocula (10^{-7} mg.) of bacilli, but did not increase very markedly the total amount of growth produced. The water-soluble ester ("Tween 80") alone did not generally permit growth of the very small inocula of human bacilli. When albumen and "Tween 80" are both present in the medium, the smallest inocula (10^{-7} mg.) of avian and human bacilli give detectable growth within eight to eleven days and fairly abundant and dispersed growth within two weeks. Cultures of mycobacteria growing diffusely in media containing 0.05 per cent "Tween 80", with or without serum albumen, have been carried through many transfers in these media without losing their viability and without any obvious modifications of their growth characteristics. The water-soluble esters of oleic acid cause mycobacteria to grow diffusely throughout the liquid medium rather than as a surface pellicle. This is believed to be due to the wetting properties of the Tween. Some long chain fatty acids are definitely toxic to the tubercle bacillus. This toxic effect is neutralized by the addition of serum albumen to the system. It may be that the beneficial effect of albumen on the growth of the tubercle bacillus—and of other microbic cells—may be due not to supplying some growth-promoting nutrient, but rather to its ability to protect the organism against an inimical environment. Results similar to the above have been obtained with 2 other human, one bovine, 12 avian and 6 saprophytic strains of mycobacteria. All avian strains tested were much more resistant than the human and bovine strains to the high concentrations of "Tween 80" and much less dependent upon the protective effect of albumen. However, the human strains were in the "rough" dissociation phase whereas the avian strains were all in the smooth phase. It is possible, therefore, that the cultural differences observed do not differentiate human and avian strains but correspond in reality to differences in the dissociation phase of the cultures used. Typical diffuse cultures of acid-fast bacilli have been obtained by inoculating positive human sputa (after treatment with sodium hydroxide), or tissues of experimental animals infected with human and avian bacilli, directly into the Tween-albumen medium. There is no indication, however, that in its present form, the medium can be utilized with advantage for the large scale cultivation of tubercle bacilli or for diagnostic work. It is probable that the medium described in the present paper is still deficient in a number of unidentified substances which are essential for optimal growth of pathogenic mycobacteria.—*Factors Affecting the Growth of Tubercle Bacilli in Liquid Media, R. J. Dubos & B. D. Davis, J. Exper. Med., May 1, 1946, 83: 409.*—(*J. S. Woolley*)

Culture Medium for Tubercle Bacillus.—The author used a basic medium of 25 cc. of Tyrode's solution. To this was added 0.5 to 1 cc. of chick embryo pulp or 1 to 2 cc. of chick embryo extract and 300 to 500 units of penicillin. The media were inoculated with transplants of stock laboratory cultures of tubercle bacilli and primary cultures of tuberculous sputum and also with material from tuberculous tissues. The cultures were incubated at 37°C. for one to four weeks. Frequent observations were made. Good growth was observed in three to eight days. The rapid growth was attributed to the embryonic tissue. The penicillin prevented contamination and also made possible repeated examination and prolonged observation of the cultures. The human type showed a prevalence of medusa head-like colonies. The bovine type showed a tendency toward formation of rather compact colonies with a few serpigenous branches. The avian type showed organisms widely scattered in loose groups often in and

around macrophages.—*Rapid Growth of M. Tuberculosis in an Embryonic Tissue Medium Containing Penicillin, I. Friedmann, Tubercle, May–June, 1945, 26: 75.—(A. G. Cohen)*

Atypical Acid-fast Microörganisms.—A preliminary qualitative study revealed that 6 strains of atypical acid-fast bacilli contained the desoxyribose type of nucleic acid when treated by the Dische reaction for desoxyribose, and that it was present in low concentration or absent entirely in 4 other strains. The present report deals with the quantitative estimation of nucleic acid in *M. phlei*, *M. thamnopheos*, 3 strains of atypical acid-fast bacilli and one strain of *M. tuberculosis hominis* of low virulence for guinea pigs. The results of this study and those of other investigators indicate that the desoxyribose type of nucleic acid is probably present in all strains of mycobacteria and that strains of known virulence for animals may have a greater content than the so-called avirulent strains. The reaction for pentose obtained with the orcinol reagent indicates that ribonucleic acid was also present in three of these strains. The nucleic acid content of 2 strains of *M. phlei* studied was found to consist largely of the desoxyribose type which differs from Coghill's finding of the ribose type. The values for the nitrogen-phosphorus ratios are consistent with that required by theory for the tetranucleotide structure of nucleic acid. The bond between nucleic acid and protein in mycobacterial nucleoprotein apparently is nonpolar since it was necessary to treat the nucleoprotein with alkali before the nucleic acid could be precipitated free of protein.—*Atypical Acid-fast Microörganisms: II. Desoxyribose Nucleic Acid Content, F. G. Petrik, J. Bact., April, 1946, 51: 539.—(F. G. Petrik)*

Growth Rate of Tubercle Bacilli.—Accurate determinations of the growth rate would be of value for the determination of the effect of physical or chemical agents on the growth of virulent tubercle bacilli. Previously such information either has been obtained subjectively, with a consequent large and unpredictable degree of error, or has been determined by the difference in total mass of culture after an arbitrary growth period. The present paper details the use of micro-Kjeldahl nitrogen determinations for the purpose of determining the normal culture cycle, the growth rate, and generation time of the H37Rv strain of virulent type tubercle bacilli. Fine suspensions of virulent tubercle bacilli will grow readily beneath the surface of synthetic media which permits the use of a uniform homogeneous inoculum. Following standardization by micro-Kjeldahl determinations each tube of synthetic medium was inoculated with 1.0 ml. of diluted suspension using a volumetric pipette. The tubes were shaken, capped with waxed paper and incubated at 37°C. At intervals following inoculation, usually every two days, a number of tubes were removed from the incubator and heated in a boiling water bath for ten minutes; to each tube was then added, at room temperature, 10 ml. of a saturated solution of potassium lauryl sulfate, and 1 ml. of a 2 per cent suspension of supercel. The tubes were centrifuged at about 3000 r.p.m. for five minutes. The organisms were washed twice with 20 ml. portions of potassium lauryl sulfate solution. After the final washing, digestion and nitrogen determinations of the entire contents of each tube were made. The results show that three types of growth curves were obtained with the virulent human type tubercle bacillus, strain H37Rv. Curve B is similar to those obtained with other bacteria when the plate count method is employed; a lag phase followed by a period of logarithmic growth and finally by a period of decreasing growth. Curves A and C, however, show that tubercle bacilli may begin immediately to grow at a constant rate. The synthetic medium used for the tubercle bacilli would theoretically be a relatively unfavorable one; therefore it was of interest that occasionally no evidence of a lag phase was obtained. It is possible, of course, that the above results might have been due to the fact that the organisms used as an inoculum had, in the case of curve B, already passed the period of logarithmic growth, whereas those used in curves

A and C were in the logarithmic growth phase at the time of inoculation. On several occasions a rapid rate of growth was noted for periods of six to eight days, followed by a sudden decrease in rate, which then remained constant for six to eight days. The method was used to determine the inhibition of growth of *M. tuberculosis* (H37Rv) by 4,4′diaminodiphenyl sulfone. The results show that when 0.05 mg. per cent was present in the medium, the rate of growth was inhibited approximately 28 per cent. With a concentration of 1 mg. per cent, the inhibition of the rate of growth was approximately 62 per cent. The addition of 1 mg. per cent para-aminobenzoic acid completely reversed the bacteriostatic action of 4,4′diaminodiphenyl sulfone and did not itself exert any stimulating or inhibitory effect on the growth of the tubercle bacilli. The method also clearly shows a lag in the inhibitory action of this sulfone on the tubercle bacillus similar to the lag action of the sulfonamides that has been observed with other bacteria. Under the conditions of the experiment the generation times of the virulent human type tubercle bacillus were found to vary between approximately one and one-half and three and one-half days.—*A Method for the Determination of the Culture Cycle and the Growth Rate of Virulent Human Type Tubercle Bacilli, G. P. Youmans, J. Bact., June, 1946, 51: 703.*—(*F. G. Petrik*)

Virulence of Tubercle Bacilli.—Natural resistance of the organism is generally recognized as the major factor in determining the course of tuberculous infection, although acquired immunity as well as virulence and quantity of the infecting agent are also important determinants. Experimental work now shows that there is a tremendous variation in the virulence of bacilli in sputa; evidence is available to indicate that tubercle bacilli may be injured in some way by the host such that their virulence and/or germinating percentage is markedly reduced. Studies of the number of bacilli in a given sputum on direct smear, concentration, culture and the type and distribution of parenteral lesions in guinea pigs after inoculation with the material warrant the following observations: (*1*) the uniformly low germinating percentage common to all sputa examined is caused by the fact that large numbers of bacilli are killed by the homogenization process with sodium hydroxide (later trials without homogenization yielded significantly higher germinating percentages); (*2*) better results obtained by culture than by inoculation (although bacilli were of standard virulence) are explained by the considerable degree of natural resistance of animals, while the culture medium offers better living conditions for injured bacilli; and (*3*) great variation in virulence of bacilli from different sputa is demonstrable. One may conclude that several tubercle bacilli may be inhaled without giving rise to a primary complex or even a positive tuberculin reaction and that not only natural resistance but virulence of the infecting bacilli and acquired immunity are of significance in the pathogenesis of infection.—*Studies on the Virulence and Germinating Percentage of Tubercle Bacilli in Sputum, K. A. Jensen & J. Bindslev, Acta tuberc. Scandinav., 1946, 20: 46.*—(*P. Q. Edwards*)

Metabolism of Tubercle Bacilli.—In 1941 the interesting observation was made by Bernheim that the addition of salicylates and benzoates increased the oxygen consumption of tubercle bacilli. When an attempt was made to repeat these experiments, it was found that tubercle bacilli of the BCG strain did not react in this fashion. This investigation was carried further with 4 strains of pathogenic human and bovine bacilli, and 5 strains of nonpathogenic human and bovine bacilli. It was found that oxygen consumption was increased by the addition of salicylates only in the case of pathogenic strains, regardless of whether they were of the human or bovine strains. Salicylate addition was without effect on the nonpathogenic strains. The question is raised as to whether benzoates and salicylates act as catalyzers or metabolites. Studies are in progress to determine if competitive growth inhibition will occur on the addition of certain salicylate compounds to

pathogenic tubercle bacilli.—*Determination of Pathogenicity of Tubercle Bacilli by Their Intermediary Metabolism, J. Lehman, Lancet, January 5, 1946, 250: 14.*—(*H. Marcus*)

Granules of *M. Tuberculosis*.—It is known that the inoculation of material free of acid-fast bacilli can cause tuberculosis in the animal. The only explanation is that *Mycobacterium tuberculosis* can, under certain circumstances, develop biochemical and morphological properties which are distinct from its bacillary acid-fast form. The author has succeeded in obtaining variations of the classic tubercle bacillus. These variations have been constant and distinct. They were obtained repeatedly in different series of experiments. With those forms Nadal could provoke by inoculation in a small number of animals typical tuberculosis with presence of acid-fast bacilli. The Koch-bacillus can exist in the tissues in the form of acid-fast or non-acid-fast granules (Ziehl-positive or Much-positive granules). These can separate from the body of the bacillus and live independently. Much-positive and Ziehl-positive granules are of the same structure but represent different phases of the metabolic development of the granules. The conception that the granular forms develop with the aging of the tubercle bacillus is erroneous. The author has succeeded to cultivate granules *in vitro*. The presence of granule-containing bacilli and free granules during the phase of proliferation of the bacillus suggests a possible intervention of these structures in the generative mechanism of the tubercle bacillus. In the beginning of a new cleavage phase the bacilli show one or several granules in their bodies. The acid-fastness of the bacilli and granules depends on the number of passages of the strain in the same medium. The more often it has been passed the higher the number of acid-fast elements. The granules begin to overlap the stroma. The stroma becomes less acid-fast and finally disappears. At this moment the granules become free. The isolated granules have a cocco-bacillary appearance and show all phases of their transition. These cocco-bacilli develop into bacilli of different lengths which are strongly acid-fast. This development shows that the granules are pre-bacillary forms which finally become homogeneous in acid-fastness and morphology. The distinct biochemical behavior of the bacilli to the Ziehl-Neelsen stain corresponds to different periods of enzymatic adaptation of *Mycobacterium tuberculosis* towards different proteins. The granules never change in character in the same strain. The tubercle bacillus forms granules only when the defense mechanisms of the body increase and create unfavorable conditions for the bacillus. That is why granular forms are found in patients who show clinical improvement. Amongst 100 patients the appearance of granular forms was accompanied by clinical improvement in 75. At the same time the acid-fastness of the bacilli diminished. In the Ziehl-Neelsen stain, they showed only pink coloration. As the acid-fastness depends on the lipoid contents of the body of the bacillus the appearance of the granules must be connected with some lipolytic action. When the blood lipase was increased and the patient showed clinical improvement, granule-containing bacilli appeared in the sputum. The action of the blood lipase and of pleural exudates on colonies of tubercle bacilli has been studied. The acid-fastness of so treated cultures diminished or disappeared completely. A totally different form of granules is observed in aged cultures which is distinguished from young granules by the absence of the bipolar form.—*Problems bilogicos que aun plantea la bacteriologia de la tuberculosis, H. Sanjuan Nadal, Publ. del Inst. Antituberculoso "Francisco Moragas", Barcelona, 1945, 6: 73.*—(*W. Swienty*)

Mycolic Acid.—Mycolic acid gives monolayers resembling the liquid-expanded type with a temperature of half expansion at 41°C. The monolayer is unstable when the area per mol. is reduced below 60 sq. Å. Mycolic acid is microcrystalline and specimens precipitated from solvents give X-ray diffraction patterns showing three side spacings of 4.58, 3.86 and 3.57 Å, respectively. Melted speci-

mens show one very diffuse side spacing of 4.2 Å and also several orders of a long spacing of 100 Å. The behavior of the substance indicates that in the latter modification the mols are vertical. The length of the mol is therefore probably either 50 or 100 Å, depending on whether the arrangement is one with single or double mols. Possibly due to inhomogeneity of the acid the tendency to crystallize is poor and no long X-ray spacing has been obtained from specimens prepated from solvents.—*A Monolayer and X-ray Study of Mycolic Acid from the Human Tubercle Bacillus, S. Ställberg-Stenhagen & F. Stenhagen, J. Biol. Chem., July, 1945, 159: 255.*—(*F. B. Seibert*)

Tubercle Bacilli and Urea.—The author reports a case of tuberculous pyopneumothorax with skin ulcerations resulting from infection of the needle tracks. The skin ulcerations were treated with dry powdered urea and healing ensued promptly. The chest fluid, after eight removals, washings-out with sterile saline and replacement with 300 cc. of half-saturated urea solution, became at last completely sterile for tubercle bacilli. Experimental work was then done on cultures of human, bovine and avian tubercle bacilli. In the course of a month all three exposed to the saturated urea solution remained apparently sterile. At a subsequent subculture from the apparently sterile capsule of human tubercle bacilli a very small growth was obtained.

However, on further trial, using a more carefully saturated urea solution, both the original capsule and the subculture remained negative for tubercle bacilli. Further observations revealed that when a suspension of tubercle bacilli in half-saturated urea solution was divided into two parts, and one part subjected to dialysis, the other not, and the two compared after forty-eight hours, it was revealed that the undialysed portion contained 55.2 g. of urea per 100 cc.; the dialysed portion 0.013 g. of urea per 100 cc. It would appear, then, that a strong suspension of tubercle bacilli, killed by forty-eight hours contact with a saturated solution of urea, can be freed of urea by dialysis and retained as a dead bacterial suspension for any purpose required.—*Tubercle Bacilli and Urea, S. L. Cummins, Brit. M. J., June 16, 1945, 1: 841.*—(*D. H. Cohen*)

Alkylresorcinols on Tubercle Bacilli.—In an earlier unreported investigation it was found that 10^{-4} per cent of 4-n-hexylresorcinol in Long's liquid synthetic medium inhibited the depth growth of 10^{-3} mg. (about 10^6 bacilli) of the H37 strain of the human type tubercle bacillus, when either n-hexylic acid to which equivalent molecular amounts of sodium hydroxide had been added or resorcinol was placed in the same medium, growth was prevented by 10^{-1} and permitted by 10^{-2} per cent concentration. It seemed desirable to investigate the antibacterial effects of other 4-n-alkylresorcinols. The bacteriological technique was the same as that used by the author in 1944 for other similar studies. The 4-n-alkylresorcinols were dissolved in sterile solutions of 30 per cent glycerol in distilled water and placed in a dark closet at room temperature. The following percentages of concentration—2 and 2×10^{-1} of ethyl, propyl, butyl, and amyl; 10^{-1} of hexyl and heptyl; and 2×10^{-2} of octyl, decyl, undecyl, dodecyl, and tetradecyl resorcinols were sterile at the end of twenty-four hours. Dilutions were made in Long's medium to give 10^{-2}, 10^{-3}, etc., per cent concentrations of the substances to be tested. Plantings of 10^{-3} mg. of well dispersed H37 bacilli were made and incubated at 37°C. for at least sixty days. Evaporation of water was nil. Three separate growth experiments were made for each tested substance with the exception of the hexyl and heptyl resorcinols for which 5 and 4 tests, respectively, were made. A check was made for the possible additive antibacterial effects of both hexylic and heptylic soaps separately on that of resorcinol. The results show that hexylic acid and heptylic acid, to which equivalent molecular amounts of sodium hydroxide have been added, prevent the growth of 10^{-3} mg. of the H37 strain in the depth of Long's liquid medium when present in 10^{-1} per cent concentration and permit growth in 10^{-2} per cent

concentrations. Resorcinol under the same conditions has the same effect. The corresponding n-alkylresorcinols with the hexyl and heptyl chains substituted for the H atom in the 4-positions of the resorcinol molecules inhibit growth at 10^{-4} per cent and permit growth at 10^{-5} per cent concentrations. Octyl, decyl, undecyl, dodecyl and tetradecyl chain resorcinols have the same order of growth-preventing power. The first four of these are more inhibiting then the corresponding fatty acids or resorcinol. Tetradecyl resorcinol has about the same growth-preventing effect as the corresponding myristic acid. Ethyl, propyl and amyl resorcinols have less growth-inhibiting power than the longer chain compounds but are more inhibiting than their respective fatty acids or resorcinol. The addition of alkyl chains to the 4-position of the greatly inhibiting sodium ethylmercuri-thiosalicylate molecule, with or without the substitution of other element for the Hg atom, may be of antibacterial importance in both *in vitro* and chemotherapeutic studies. Bactericidal effects were not studied.—*Growth Inhibition of Strain H37 of the Human Tubercle Bacillus by 4-n-Aklylresorcinols in the Depth of a Liquid Synthetic Nonprotein Culture Medium, W. F. Drea, J. Bact., April, 1946, 51: 507.*—(*F. G. Petrik*)

Biological Changes in *M. Ranae*.—(I) *Production of sulfonamide-resistant strain of Mycobacterium ranae:* The authors describe the development of a sulfonamide-resistant strain of *M. ranae* by serial transfer through Long's medium containing increasing concentrations of the drug. The resistant strain differs from the parent strain in many important respects including growth rate, discoloration of the medium, and the production of diazotizable arylamine. (II) *Sulfonamide resistance and susceptibility to antibacterial agents:* Experiments were designed to determine whether there were any differences in the susceptibility of the parent strain and the resistant strain of *M. ranae* to agents other than the sulfonamides. The cylinder-plate method used in penicillin assay was found satisfactory for demonstrating the comparative effects of various agents. The plate method, being dependent upon the diffusibility and bacteriostatic power of the agent, is not a measure of germicidal efficiency. However, for the purpose of comparing the resistance of the two strains of *M. ranae* to the various agents, the method is simple and satisfactory. A sulfonamide-resistant strain of *M. ranae* was found to be nonspecifically more susceptible to antibacterial agents (antagonistic environment) than its parent sulfonamide-susceptible strain. It is suggested that this is in some way associated with its slower growth rate. The rates of multiplication of microörganisms should be considered in the comparison of the susceptibilities of various strains to anti-bacterial agents or other unfavorable environmental factors. (III) *Sulfonamide resistance and para-aminobenzoic acid antagonism:* Parent susceptible and resistant strains were tested for their susceptibility to bacteriostasis by PABA. The growth rate of the parent susceptible strain in Long's medium was reduced to approximately one-half that of the controls by a concentration of 400 mg. per cent PABA; on the other hand, the sulfonamide-resistant strain was almost completely inhibited by the same concentration of PABA. This difference in the behavior of the susceptible and resistant strains remained constant after repeated transfers of the organisms over a period of seven months. It was not possible to produce a change in the susceptibility of *M. ranae* to bacteriostasis by PABA or to sulfonamides by repeated transfers in a medium containing large amounts of PABA.—*Biologic Changes in Sulfonamide-Resistant Mycobacterium Ranae, D. Yegian, V. Budd & G. Middlebrook, J. Bact., April, 1946, 51: 479.*—(*F. G. Petrik*)